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CATALYTIC ACTION

BY

K. GEORGE FALK

HARRIMAN RESEARCH LABORATORY
THE ROOSEVELT HOSPITAL
NEW YORK

Author of "The Chemistry of Enzyme Actions," "Chemical Reactions"

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PREFACE

In order to treat the phenomena of Catalytic Actions in a systematic manner, it is necessary to define or describe in some way the relations which are to be included. At the same time such a definition or description must recognize a definite connection and interrelation with chemical reactions in general. Fundamentally, the same general laws and regularities must hold for all such reactions, but Catalytic Actions are distinguished by certain peculiarities which have made it advisable to consider and treat them as a separate group.

It is the purpose of this book to emphasize the chemical nature of so-called Catalytic Actions. The general theory of the Mechanism of Chemical Reactions elaborated to some extent elsewhere serves as the groundwork. The reactions which are, by more or less common consent, included under Catalytic Actions, are then determined by the introduction of a simple concept.

Such a development is simple in principle. At the same time, the expression of certain doubts may be permitted in this connection. The various attempts which have been made in the past to define the terms Catalysis and Catalytic Action have been unsatisfactory in that the limitations imposed upon the chemical reactions and the changes involved, have been inadequate in one way or another. The writer naturally believes that the definition which he suggests for Catalytic Action is more satisfactory than any heretofore proposed, but the uncertainties of this definition are also pointed out in the pages following. In fact, it may be asked whether the separation of Catalytic Actions from Chemical Reactions in general is not an artificial one, and incapable of exact formulation. This question is discussed in some detail. The main point, however, cannot be emphasized too frequently; namely, that chemical (and also physical) relationships and laws which apply to Chemical Reactions, necessarily must hold for Catalytic Actions, no matter how these may be limited or defined.

No attempt has been made to present all the reactions or even a large number of the reactions which might be included in the phenomena under discussion. A more or less definite viewpoint is presented with sufficient examples to illustrate the general principles.

The writer wishes to thank those who have aided him in one way or another to develop his views and make possible their presentation. The manuscript was gone over, either wholly or in part, by Professor Jacques Loeb and Dr. J. H. Northrop of the Rockefeller Institute for Medical Research, and by Professor George B. Pegram of Columbia University, and some changes were incorporated as a result of their suggestions. The various relations were clarified and elaborated greatly in consequence of discussions with Professors J. M. Nelson, Ralph H. McKee, and H. T. Beans of Columbia University. Finally, the writer wishes to express his indebtedness to Miss Grace McGuire and Miss Helen Miller Noyes, his associates at the Harriman Research Laboratory, for their constant co-operation and invaluable aid in the writing of this book as well as in its preparation for publication.

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CATALYTIC ACTION

Chapter I.

Introduction: General Views on Catalysis.

The science of Chemistry may be said to deal with (1) the properties and compositions of substances; (2) changes in these properties and compositions which accompany interactions between various substances; and (3) changes which take place under the influence of changes in external conditions. The expression of the laws and regularities which are involved in such properties, compositions, and changes, forms the main problem of chemistry.

The so-called physical properties of substances and mixtures, such as crystal form, fusion temperature (or melting point), vapor pressure, specific gravity (or density), color (light absorption and reflection), heat conductance, electric conductance, etc., may be determined by suitable measurements directly on the substances themselves. In order to determine the chemical compositions of substances, or to find their relations to other substances in the sense that certain reactions or phenomena are common to both and therefore indicate a common constituent, it is necessary to submit the substances in question to treatments which cause changes in them. Such treatments and the changes in composition, and consequently properties, of certain constituents are included under the general term "chemical reactions." It is, therefore, fairly obvious that the study of chemical reactions is one of the most important of the problems which can be taken up in connection with the science of chemistry. The determination of the compositions of substances depends upon chemical reactions, the estimation of various constituents, the formation of various products, and in fact practically every change which

is reflected in a change in properties involves in one form or another a chemical reaction. Chemical reaction always involves change. It is dynamic in nature and is as a rule of greater complexity, and perhaps, therefore, of more profound interest, than the static side of chemistry.

Recently the writer published a treatise on "Chemical Reactions; Their Theory and Mechanism," [1] in which a general theory of chemical reactions was developed, based primarily upon the "addition compound formation" view. A number of the more modern concepts of chemistry were used and it was shown that this theory or viewpoint permitted the inclusion of all chemical reactions, those classed heretofore as organic as well as those included under the group inorganic. Various new relations were pointed out as following from this method of treatment of chemical reactions.

Since the importance of chemical reactions is so great in chemical practise and theory, it is of interest to follow some of the lines which have been developed in this field in the course of the past hundred years. The present book is an attempt to present a group of reactions which has been separated from the group of chemical reactions in general and treated as a special class showing certain distinctive relations. At the same time, the more general points of view applicable to all chemical reactions will be retained here and emphasized wherever possible.

Catalytic actions have been grouped for a number of years as a distinct class of chemical reactions having certain properties or relations in common. The importance which has been ascribed to them is evident from the number of publications, both in the form of books and of articles, which have appeared and are still appearing. They will not be taken up here from the point of view of their own distinctive behavior primarily, but rather, their relations to chemical reactions in general will be described and the points discussed in which they are supposed to differ from these. In this way it is hoped to show the relations of catalytic reactions to other reactions and in a measure to unify the phenomena of chemistry in place of creating new branches or subdivisions. Also, it will be seen that catalytic reactions exemplify certain relations which are not as apparent in other reactions.

[1] The D. Van Nostrand Company, New York, 1920.

In this way a study of such reactions may extend and strengthen the concepts of chemical theory.

In studying a certain group of reactions such as catalytic reactions, which are separated from reactions in general because of possessing certain properties or characteristics or showing certain behaviors, it is first of all necessary to state what these properties or characteristics or behaviors may be, or in other words, to define as accurately as is possible the meaning of the term catalytic reaction or catalysis. An accurate definition would simplify greatly the study of the problem, while a definition or description which speaks in more or less general terms of the phenomena in question will lead to greater or less uncertainties in the treatment. In the following considerations, it will be pointed out that the definitions which are generally given for catalysis and catalytic actions have developed in a gradual manner; that the phenomena which have been included were frequently not well characterized, and in fact often not characterized at all; that a somewhat top-heavy theoretical structure has been developed in which an increased knowledge of the mechanism of certain reactions did not aid materially in the general views on catalysis; and that finally, the consideration of catalytic reactions as compared with other reactions, may be shown to lead to a simple definition which appears to be of general applicability.

The conception of catalysis was introduced into Chemistry in 1836 by J. Berzelius in order to group together a number of apparently diverse chemical reactions and to indicate that the mechanism of these reactions might be ascribed to a common cause. The reactions which he considered included the change of starch into sugar in the presence of dilute acids, the acid remaining unchanged;[1] the decomposition of hydrogen peroxide with evolution of oxygen in alkaline solution in the presence of manganese, silver, platinum, gold, or fibrin;[2] the oxidation of ethyl alcohol to acetic acid by finely divided platinum;[3] the spontaneous combination of hydrogen and oxygen in the presence of cold spongy platinum;[4] the same reaction in the pres-

[1] J. Kirchhof, *Schweigger's Journ. 4,* 108 (1812).
[2] J. Thénard, *Ann. Chim. Phys. 9,* 314 (1818).
[3] E. Davy, *Phil. Trans. 100,* 108 (1820).
[4] J. W. Döbereiner, *Schweigger's Journ. 34,* 91 (1822); *38,* 321 (1823).

ence of heated gold, silver, or glass;[1] and finally, the conversion of alcohol into ether in the presence of sulfuric acid.[2]

The views of Berzelius, based upon the study of these reactions may be best given in his own words.

"It is then proved that several simple and compound bodies, soluble and insoluble, have the property of exercising on other bodies an action very different from chemical affinity. By means of this action they produce, in these bodies, decompositions of their elements and different recombinations of these same elements to which they themselves remain indifferent.

"This new force, which was hitherto unknown, is common to organic and inorganic nature. I do not believe that it is a force quite independent of electrochemical affinities of matter; I believe, on the contrary, that it is only a new manifestation of the same; but, since we cannot see their connection and mutual dependence, it will be more convenient to designate the force by a separate name. I will therefore call this force the *catalytic force* and I will call *catalysis* the decomposition of bodies by this force in the same way that one calls by the name analysis the decomposition of bodies by chemical affinity.

"The body, which brings about the changes in the constituents, does so not by itself taking part in the new compounds; it remains unchanged and acts therefore by means of an internal force, whose nature is still unknown to us, at the same time that its existence is made known in this way.[3]

"Certain bodies exert by contact with other bodies an influence such that a chemical effect ensues, compounds are destroyed or formed afresh, without the substances, whose presence brings this about, taking part to the slightest degree.

"This force is exerted more generally, but more mysteriously, in the processes of organic chemistry, especially in living bodies; generally there appears to be no other probable reason for the manifold products which are formed in the living plant or animal from one and the same common fluid which is brought in contact with the different parts, except that the solid parts cause different changes in different places in the constituents of the added fluids. . . ."[4]

In considering the views of Berzelius it must be remembered that the concepts of "force" and of "chemical affinity" were not as clear and well defined at the time he developed the classification of catalytic actions as they are at the present time. The importance which must be ascribed at the present time to Berzelius' definition and description lies in the fact that the criteria which he used to determine whether a reaction is to be classed as catalytic are essentially those which the majority of chemists still use for the same purpose. Only if catalytic reactions are considered as a group, are more general and more exact relations

[1] P. L. Dulong and J. Thénard, *Ann. Chim. Phys.* (ii) *23*, 440; *24*, 380 (1823).
[2] E. Mitcherlich, *Pogg. Ann. 31*, 273 (1834).
[3] *Jahresber. d. Chem. 1836*, 237.
[4] Lehrbuch der Chemie, V. Edition, 1843, Vol. 1, pp. 111-2.

used. For the general descriptive relations, most chemists have not gone beyond the views of Berzelius. In studying the reactions given and the statements of Berzelius it is evident that the reason for this lies in the fact that the common cause for separating catalytic reactions from chemical reactions in general is taken to be the confession of ignorance of the nature and mechanism of the reaction in question.

This conservatism of many chemists does not mean however that advances have not been made in the classification of catalytic actions, the theoretical concepts involved, and the relations to other chemical and physical theories. Striking advances have been made, especially by Ostwald, Bredig, van't Hoff, and others, but these advances are very frequently ignored in the general chemical literature. If this is the case, it would appear that the advances were not fundamentally sound, or if sound, not useful. Although this may not be the best place to discuss the question, and also perhaps anticipates the later discussions of catalytic reactions, it may be asked whether this classification of reactions based upon an unknown factor has served a useful purpose. The answer to this question must be an unqualified affirmative. It has been possible to group a number of apparently unrelated reactions and has focussed attention upon the importance of these reactions. Whether or not this classification is of permanent use and value is of secondary significance. That further developments resulted in calling attention to the illusory nature of the unknown general relationship, that the term catalysis for a time became in a sense a term of disrepute, signifying ignorance in place of knowledge of the nature of the reaction associated with it, is of interest in the historical development. Using catalysis to call attention to unknown factors in chemical reactions often temporarily relieved the minds of those applying the term, but the real result has been to call attention to the puzzling nature of the problem involving the mechanism of the given reaction. If after reviewing some of the different aspects of the problem, it should appear to some that it would be advisable no longer to use the term catalysis, this should not be taken in any way as belittling the great service which the concept has rendered in the past, or the truly remarkable insight of Berzelius and others in developing catalytic relations in various directions.

The subject of catalysis may be studied in several different ways. One of the most interesting would be to adopt the definitions and descriptions given by Berzelius and describe the state of chemical knowledge and theory of his time. Then the views of the present time might be given, and the significance of catalysis as at present understood. Such a presentation would involve giving the theoretical conceptions of chemistry of the two periods as they bear upon catalysis. These two cross-sections of chemical knowledge and theory centered upon catalysis would necessarily develop into a historical comparison of the chemical knowledge of the periods of 1840 and of 1920 as related to catalysis. This would furnish interesting matter for discussion but it would hardly be profitable in the present connection to enter minutely into such a comparison. The danger would lie in giving a one-sided historical view of the two periods in such a presentation, since necessarily many problems and theories might have been developed which apparently were not related at the time to the problem in question and would therefore have been omitted. Also, the views held at present by different workers do not agree in all particulars, and the presentation would consist of a comparison of a fairly accurate historical view of the older period with a more or less personal view of the present period.

A second method of treating catalysis would be the encyclopedic method which involves a complete and detailed account of catalytic reactions including the historical development. Such treatments have been given at different times, either covering the greater part of the field of reactions and theories which have been taken up in connection with catalysis, or dealing with more or less specialized subdivisions of the field which have been suggested at various times. It would be invidious to single out any special treatment for reference.

Since this field has been covered in a satisfactory manner, there does not appear to be any reason at present to add another compilation to the list.

Another way of treating the subject of catalysis is to take up separate topics, each including a number of related or similar reactions, and discussing the relations separately. Thus, the following topics might be chosen to describe the general phenomena of catalysis.

Catalytic actions connected with hydrogen ions.
Catalytic actions connected with hydroxyl ions.
Catalytic oxidation-reduction actions.
Catalysis in homogeneous solutions.
Catalysis in heterogeneous systems.
Enzyme actions.
Etc., etc.

Such a presentation would include a somewhat detailed discussion of reactions more or less typical for each group as well as the general characteristics of the different groups. Many valuable points might be obtained in this way, but the weakness of this method of presentation lies in the fact that after characterizing the predominating features of each group, when comparing the different groups with each other, attention is likely to be drawn to the differences shown by the various subdivisions. Since attempts at advance in the scientific treatment of chemical phenomena appear to be more useful if similarities are brought out and apparently diverse phenomena correlated, dividing the field of catalytic actions into a number of smaller groups, while useful in some ways, will only be adopted secondarily in the present instance.

From what has been said so far, it may be seen that the object here is to define as accurately as is possible the group of catalytic reactions; to show the relations of these catalytic reactions to chemical reactions not included under catalytic; and to find, if possible, general relations underlying the cause or mechanism or whatever it may be called, of these reactions.

The method of treatment to be adopted appears to reverse the traditional, time honored method of considering chemical phenomena and theories. In place of describing a large amount of data and facts and developing hypotheses and theories from these, general viewpoints will be adopted wherever possible, and relations to other branches of science will be indicated. At the same time as many illustrations as practicable will be given. This is not an elementary treatise of catalytic actions. The reader is assumed to be sufficiently familiar with general chemical reactions to fill out the necessary details.

In this chapter, the general status of the views held with regard to catalytic actions is being presented. The development of these views is marked by two outstanding conceptions. The first was that of Berzelius in which the term catalysis was pro-

posed to include the phenomena in which a chemical reaction takes place, in some way because of the presence of a substance apparently not involved in the reaction. The second great theoretical advance was due to W. Ostwald who in 1894 and the succeeding years developed the significance of reaction velocity in catalytic phenomena. "Catalysis is the acceleration of a slowly proceeding reaction by the presence of a foreign body. . . . There are numberless substances or combinations of substances, which are in themselves not stable, but in a state of slow transformation and therefore appear to be stable, because their transformations take place so slowly that they are not appreciable in the short time of observation generally employed. Such substances or systems frequently attain an accelerated rate of transformation, if certain foreign substances, i.e., substances not necessary for the reaction itself, are present. This acceleration occurs without change in the general energy relationships, since after the reaction is completed, the foreign substance can be considered to be removed from the reaction sphere, so that the energy which may have been used up in adding it is regained by its removal, or the reverse. The changes must, however, as in all natural transformations, occur in the sense that the free energy of the whole system decreases. It is misleading, however, to look upon catalytic action as a force, which brings about something which would not take place in the absence of the catalytically active substance." [1]

The typical examples of catalytic actions which may be mentioned in this connection include the hydrolysis of esters, of sucrose, and of acetamide by acids, different acids producing different changes in velocities, but the acid producing each effect being unchanged at the end of the reaction. A great part of the experimental data bearing upon these reactions was due to Ostwald.[2] It remained for Arrhenius to show that these catalytic actions of acids might better be referred to the actions of the hydrogen ions formed by the electrolytic dissociation of the acids. This last was a great step forward in the correlation of the experimental data, and it has only been in recent years that the view of the catalytic actions of hydrogen (and also of

[1] W. Ostwald; review of an article by F. Stohmann, *Z. physik. Chem.* **15**, 705 (1894).

[2] W. Ostwald, *J. pr. Chem.* **27**, 1; **28**, 449 (1883); **29**, 385; **30**, 93 (1884).

hydroxyl) ions was shown to be incomplete and to necessitate modification. This question will be taken up again in a later chapter. It may also be pointed out that the experimental studies of G. Bredig and his co-workers added considerably to the quantitative knowledge of various catalytic reactions.

Berzelius had given a qualitative meaning to the term catalysis; Ostwald gave it a quantitative meaning. Following Ostwald, it was possible to give quantitative measurements in connection with catalytic phenomena and to fix the significance of the terms more satisfactorily. This advance was only possible because of the advance in chemical theory in connection with chemical affinity and its measurement, and because of the experimental and theoretical studies of reaction velocities or chemical kinetics which had systematized the relations and had successfully applied mathematical equations to chemical equations in so far as the rates of change of the reactions represented by these equations were concerned. The views brought out and elaborated by Ostwald in various publications accepted the proposition of Berzelius that a chemical reaction took place in the presence of a foreign body known as the catalyst. He added thereto the proposition that the velocity of a chemical reaction was changed by the presence of the foreign body, foreign in the sense that it apparently did not take part in the reaction, or in other words, that it appeared at the end of the reaction apparently unchanged as compared with its condition at the beginning of the reaction.

It is of interest historically in connection with the advance made by Ostwald in the theoretical treatment of catalytic actions to note that Wilhelmy [1] in his study of the action of acids on sucrose in which the law of mass action was formulated and applied quantitatively for the first time, stated "I must leave it to the chemists to decide, whether and how far the formulas obtained are applicable to other chemical processes; in any case, all those processes to which one ascribes the operation of a catalytic force seem to me to belong to this class."

The terms "catalytic action," "catalytic forces," "catalysts" or "catalyzers," following the classification of Berzelius and as modified in a number of minor particulars by other workers in

[1] L. Wilhelmy, *Pogg. Ann. 81*, 413, 499 (1850).

this field, were used in a more or less indeterminate way to include a number of chemical reactions which were influenced in an unknown manner by substances present but apparently not involved in the reactions. For a number of years, and in fact frequently at the present time, the advances in chemical theory were not used in connection with catalytic reactions or in denoting a reaction as catalytic. As a natural result, these reactions and the term catalytic actions became known as a sort of general group of reactions to which any unknown factors in the mechanism of chemical reactions were ascribed. The scientific knowledge of such reactions was therefore not advanced, and in fact in a number of cases it was retarded, by the camouflaging of the ignorance represented by the term "catalytic." Thus, in the recent monograph of S. C. Lind,[1] one of the reasons for the slow development of Photochemistry was stated to have been "the early unfortunate over-emphasis of the *catalytic* nature of photochemical phenomena."

The reason for this unfortunate development in catalysis cannot be ascribed to the classification outlined by Berzelius, who advanced chemical theory in this particular as in many others, but rather to the blind following of those who used his views without considering the advances which had taken place both in the more extended knowledge of the mechanism of reactions and in the theoretical viewpoints which had been developed. As stated, it remained for Ostwald to put the views on catalysis on a more definite and satisfactory basis by pointing out the significance of reaction velocities. The more detailed discussion of reaction velocities in relation to catalysis will be presented in the following chapter.

As a result of the large amount of experimental work which was accumulated under the general heading of catalysis, certain criteria were developed which were considered necessary for a reaction to be placed definitely in the indicated category. As it is desired to present in this chapter an outline of the views on catalysis which are held more or less commonly at present, these criteria will now be stated as given in one of the most satis-

[1] S. C. Lind, "The Chemical Effects of Alpha Particles and Electrons"; American Chemical Society, Monograph Series. The Chemical Catalog Co., Inc., New York, 1921. Page 19.

factory of the recent books on the subject.[1] Omitting the detailed discussion given by the authors, they are as follows:

"(1) The chemical composition of the catalytic agents is unchanged on completion of the reaction process.
"(2) Minimal amounts of a catalytic agent are adequate for the transformation of large quantities of the reacting substances.
"(3) A catalyst cannot affect the final state of equilibrium.
"(4) A catalyst modifies the velocity of two inverse reactions to the same degree.
"(5) A catalytic agent is incapable of starting a reaction; it can only modify the velocity of the reaction."

It is shown that on the basis of thermodynamics, criteria (3) and (4) follow from (1) and (2); that as a corollary from (3) and (4), "it follows of necessity that the state of equilibrium is independent of the nature and quantity of the catalytic agent."

In the later chapters of this book an attempt will be made to show the applications and some of the possible limitations of these criteria. The topics will not be taken up consecutively, but the general discussion may serve to show the relations without taking up each point separately. At the same time, while these criteria are given as the result of the careful study of a large number of reactions and have been accepted in general terms for a period of years (fifteen years or more) a review of the articles on catalytic reactions even of recent years does not indicate that the criteria have been taken into account in the classification and consideration of many of these reactions. Only in isolated cases, has the treatment been guided by the various criteria. The classification generally used is essentially that of Berzelius with the addition of the change in velocity as postulated by Ostwald. This cannot be due alone to the failure of chemists to adopt the theoretical developments, but may be more probably ascribed either to the inadequacy of the theoretical views, or to the indefiniteness of the definitions, or to the multiplicity of criteria or requirements involved in the classifications. This question will be developed further in later chapters.

In various treatments and compilations of catalytic actions, attempts have not been lacking to present classifications of catalytic reactions and reagents in order to systematize the relations.

[1] E. K. Rideal and H. S. Taylor; "Catalysis in Theory and Practice," Macmillan & Co., Ltd., London, 1919. Chapter I, on "Criteria of Catalysts."

None of these systems of classification has been found entirely satisfactory. In order to show their nature, that developed by Ostwald [1] will be outlined:

I. Crystallization from supersaturated solutions. E.g., the crystallization of sodium sulfate from a supersaturated solution in the presence of a flake of dust or the fragment of a crystal.
II. Catalyses in homogeneous systems. E.g., the action of acids upon aqueous solutions of cane sugar.
III. Catalyses in heterogeneous systems. E.g., the action of platinum upon a mixture of air and sulfur dioxide gases.
IV. Action of enzymes. E.g., the action of emulsin upon amygdaline.

It might appear that groups II and III include all the necessary reactions, and that the other two groups are merely subdivisions of these, although it appears difficult to classify the phenomena of group I as chemical reactions.

The most obvious criticism of such a system of classification is that for example, groups II and III do not appear to be dependent upon reactions as catalytic but are applicable to all chemical reactions. No special criterion of catalysis is involved.

The question of the part played by a solvent in connection with a reaction taking place between dissolved substances has been discussed frequently. The velocity of a chemical change may be altered considerably because of the specific nature of the solvent. The changes occurring in aqueous solutions furnish, of course, the most common and best known examples. Other solvents may, however, exert specific actions as well. Thus, the rate of transformation of ammonium cyanate into urea was found to be thirty times as great in ethyl alcohol as in water.[2] Ostwald [3] clearly recognized the fact that solvents should be regarded as catalysts and that there is no difference in principle between a small amount of substance acting as a catalyst, or a large amount (as with a solvent). Van't Hoff,[4] however, including the criterion of unchanged equilibrium in his description of a catalyst, pointed out that the effect of a medium, such as the solvent, on a catalytic action may make itself evident in one of two ways. In the first place, the solvent (or medium) may affect the two opposing actions of a reversible reaction in the

[1] W. Ostwald, *Z. Elektrochem.* 7, 995 (1901); *Nature* 65, 522 (1902).
[2] J. Walker and S. A. Kay, *J. Chem. Soc.* 71, 489 (1897).
[3] W. Ostwald, *Z. Elektrochem.* 7, 998 (1901).
[4] J. H. van't Hoff, "Lectures on Theoretical and Physical Chemistry," translated by R. A. Lehfeldt, 1899, Vol. 1, p. 221.

same way and consequently have no influence on the final state of equilibrium; and in the second place, the solvent may exert a specific action depending upon the relation between the solvent and each of the reacting substances. Van't Hoff showed how the disturbing effect of the solvent on the state of equilibrium might be eliminated theoretically.

The possible action of the solvent as a catalyst has been indicated because of the number of reactions which occur in solutions, and to bring out the fact that whether or not the solvent is assumed to act as a catalyst, and the consequent theoretical deductions, depends essentially upon the definition of catalyst which is adopted. This fact will appear in other connections as well.

Catalytic actions are extremely common. Ostwald stated that "There is probably no kind of chemical reaction which cannot be influenced catalytically and there is no substance, element or compound, which cannot act as a catalyzer." The widespread character of the chemical changes which have been included under catalytic reactions accounts for the difficulty of developing a simple classification of catalytic actions which would be different from, or at least not dependent upon, the classification of chemical reactions in general. A number of theories of catalytic actions have been suggested at various times dealing with separate groups of reactions and accounting for these in a more or less satisfactory but isolated manner. No general viewpoint appears to have been developed in this way which would include catalytic phenomena as a whole, separate from, even if related to, other chemical reactions. It seems to the writer that a more satisfactory result might be obtained if it were possible to develop a viewpoint which would include all chemical reactions, including those classed heretofore as catalytic, without calling attention primarily to the special attributes which are taken to predominate in the classification of catalytic reactions. This would mean that the mechanism of chemical reactions in general is the main factor involved, that certain regularities and principles applicable to all reactions might be developed from such a study, and that catalytic reactions would form a special group in such a system in which certain conditions may be fixed, but where the phenomena at the same time obey

the general laws observed with chemical reactions as a whole. This view will not be developed farther here but will be brought out in greater detail in Chapter III.

The industrial applications of catalytic actions can only be referred to briefly. The catalytic reactions which have been used and are being used in this way are so numerous that a mention of a few of those which are specially prominent at the present time is all that can be attempted. Thus, the various processes of sulfuric acid manufacture, including the contact process, the Haber and the Claude ammonia processes, the various hydrogenation processes for fats and oils, the oxidation reactions such as the conversion of ammonia into nitric acid, the Deacon process for chlorine, and the production of phthalic acid from naphthalene by sulfuric acid in the presence of mercury or other metals, the saponification of oils (Twitchell process), the dehydration of alcohol to form under certain conditions unsaturated hydrocarbon and under different conditions ether, and the combustion reactions taking place in the presence of mixtures of various metallic oxides such as those used in incandescent gas mantles, are a few in which catalytic reactions in one way or another play a predominating rôle. Certain enzyme actions are also to be included.[1] Reference will be made in the following chapters to the phenomena occurring in some of these reactions, not from the point of view of their industrial significance, but rather as bearing upon certain questions of general interest in the classification and explanation of the reactions.

[1] Cf. K. G. Falk, "The Chemistry of Enzyme Actions," Chapter IX, "Uses and Applications of Enzymes."

Chapter II.

Reaction Velocity and Catalysis.

It was stated in Chapter I that the outstanding advance in the development of the views on catalysis, following the pioneer work of Berzelius was the introduction of the concept of reaction velocity by Ostwald. Ostwald defined catalysis as the acceleration of a chemical reaction by the presence of a substance which is itself unchanged as a result of the reaction. The theoretical bases of reaction velocity had been given a firm foundation by the study of the kinetics of a number of chemical reactions and the application of mathematical equations, in the integrated as well as in the differential forms, to represent the velocities under different conditions. The possibility of considering catalytic actions from a quantitative point of view marked a distinct advance in the treatment of these reactions. In this chapter, an attempt will be made to present some of the principles upon which chemical kinetics are based, and certain limitations in their application to catalysis.

Before doing this it may be pointed out that the view of change in reaction velocity has been recognized by most workers as an essential part of catalysis. Thus Bredig [1] considered catalysis to consist of the acceleration of a slow chemical reaction by means of the presence of a foreign body. Stieglitz [2] went farther. He considered that the only fundamental fact common to all catalytic actions, or the characteristic of such actions, is an acceleration in the rate of reaction and that further deductions in connection with catalysis are merely applications of the fundamental laws of chemistry. The views presented in these contributions will be taken up again later in this chapter.

With regard to the general kinetic relationships which have

[1] G. Bredig, *Ergebnisse der Physiologie, I,* 134 (1902).
[2] J. Stieglitz, *Proc. Congr. Arts and Sciences,* St. Louis, 1904, Vol. IV, pp. 276-84; *Am. Chem. J. 39,* 63 (1908).

been developed and applied with a number of reactions, this is not the place to enter into the details. Such expositions may be found in a number of publications devoted more specifically to these problems. Reference can be made here only to such questions as the numbers of molecules taking part in reactions or the orders of the reaction including methods of their determination, the influence of external factors such as temperature and pressure, etc. At the same time, it must be emphasized that for a proper and satisfactory understanding of the relations involved, the mathematical deductions and equations are absolutely essential. They are not repeated here, except for the purpose of bringing out definite points, because of the necessary limitations of space, since an incomplete presentation is even less satisfactory than none at all.

In order to develop some fundamental points in connection with chemical kinetics, the following brief outline will be presented. In the development of the mathematical equations representing the kinetics of chemical reactions, the general expression may be put in the form

$$v = k\, c_1\, c_2 \ldots . c_n, \qquad (1)$$

in which v represents the velocity of the reaction, or the change in concentration of the substances, c_1, c_2,.... in unit time at constant temperature, each c term representing one of the substances undergoing change. The symbol v would be given in more exact mathematical form as the differential expression $-\frac{dc}{dt}$ which represents the rate of change of the concentration of one or more of the substances c_1, c_2,.... The term k represents the proportionality constant, characteristic for the reaction in question under the given conditions. The integrated expression of equation (1) (as a differential equation) is used in the practical tests in chemical kinetics.

Equation (1) and the expressions derived from it are based primarily upon the law of mass action. This raises at once several pertinent questions. Some of these were taken up in another connection.[1] The following quotations will serve to

[1] "The Chemistry of Enzyme Actions," K. G. Falk, American Chemical Society; Monograph Series. The Chemical Catalog Co., Inc., New York, 1921. Chapter II.

illustrate the significance of the theoretical basis underlying equation (1)[1]

"The law of mass action forms the basis of the exact study of chemical kinetics. This law states that the amount of substance undergoing change in a unit of time is proportional to the active mass present during that time. This law is of general applicability. In applying it in chemical reactions, it is obviously necessary to use certain units of mass or quantity in order to determine the active mass of substance present at any given time. The simplest view to take is that the active mass of a substance is given by its molecular concentration. For practical purposes, therefore, the number of gram molecules or mols per liter of volume will be used as the active mass.

"Before going further, however, it is necessary to emphasize the simplification which has been introduced. The active masses have been replaced by molecular concentrations, and therefore, the law of mass action has been changed to the law of concentration action. If, now, deductions from the law of concentrations are found not to be valid, this does not mean that the law of mass action does not hold, but that an incorrect hypothesis may have been introduced in the substitution of concentrations for active masses."

The relation between the chemical equation and the mathematical equation deserves consideration. The chemical reaction may be represented by an equation of the form

$$A + B + \ldots. = L + M + \ldots. \qquad (2)$$

This equation indicates the transformation of the substances whose chemical compositions are given by *A, B,* .... into the substances whose chemical compositions are given by *L, M,*.... and the relative amounts of the substances changed. Nothing is shown by the chemical equation beyond this. The rate of reaction, the energy change, and, in general, the mechanism of the chemical reaction is not shown by the chemical equation. The chemical equation as ordinarily written only shows the substances whose chemical compositions have been changed and the chemical compositions of the resulting substances. Any number of substances not shown in the chemical equation may have taken part in the chemical reaction, but as long as their chemical compositions are unchanged in the final state of the reaction, they are not included in the chemical equation. Also, the chemical equation ordinarily does not show the mechanism of the reaction, whether the reaction takes place in two or more stages, possibly involving other substances without changing their compositions.

[1] L. c. p. 20-21.

These limitations of the chemical equations must be borne in mind in discussing the theoretical, and also the practical, aspects of the mechanisms and the velocities of chemical reactions. The chemical equations show only the compositions of the changing substances and the masses involved. In combining the chemical equations with the kinetic equations, these limitations must be included in the deductions and conclusions.

The limitations inherent in the original expression must necessarily be found in the final integrated equation. The chemical limitation is that of considering only the substances whose compositions finally are different from the compositions of the substances initially. Other substances are not, as a rule, represented in the chemical equations, and, consequently, are not included in the kinetic equations. This leads at once to several important reservations in the use of the chemical equations. It is readily conceivable that a substance takes part in a reaction but retains the same composition at the end of the reaction as it had at the beginning. Such reactions will be referred to frequently in this book. For one thing, the great group of reactions which take place in solvents such as water, may be quoted. In the absence of the water, the reactions apparently do not take place; in its presence, they take place readily. The water must play some part, but it is generally omitted in writing the chemical equation. Also, one of the criteria of a catalyst is an unchanged composition, and such reactions would therefore be included in this group. This question will be taken up in more detail in the following chapter.

Closely connected with these factors is the possibility of the reaction taking place in two or more stages. Here, if one of the reaction steps takes place rapidly and the other slowly, it will be the velocity of the slow reaction which is being measured experimentally, although the chemical analyses of the initial and final products would throw no light on the relative velocities in the two stages. The kinetic equation would then give values for the constant indicating that the reaction was proceeding according to the mechanism assumed in the complete chemical equation when actually only the slowest step of a series of successive changes is being measured by the kinetic equations. This is unquestionably true for almost all reactions which take place

in aqueous solution where the water is not assumed to take part directly in the actions.

One point must, however, be mentioned in this connection. If the concentration of one of the reacting constituents present during a reaction is so large that during the period of time that the reaction is under observation the change in its concentration is small compared with the amount present, then the application of the kinetic equations will apparently indicate that it is not taking active part in the reaction. This means that the experimental methods under such conditions will not reflect the (comparatively) small change in concentration of this constituent.

To return to equation (1), the constant k when found by the use of the suitable integrated kinetic expression from a series of experimental measurements of a chemical reaction at different intervals during its course, is taken to be characteristic for this reaction under the definite conditions at the temperature in question. Rise in temperature increases the value of k greatly; two to three-fold for a 10° increase. Any change in the reaction mechanism or the conditions under which the reaction is taking place would show itself in a changing value of k. In general, a constancy of k as determined experimentally under definite conditions is taken to be satisfactory evidence that the reaction in question follows the course assumed in the chemical equation. If a change in phase occurs in the course of the reaction, such as a gas being evolved or a solid precipitated, or if a reaction takes place at the boundary of two phases, entirely misleading conclusions may be drawn from a consideration of the kinetic results. Under such conditions, the measurements often represent only a diffusion rate, and the mathematical expression found to hold would be similar in form to that representing a monomolecular reaction rate.

The definition of Ostwald of a catalytic action involves an increase in velocity by the presence of a substance which is unchanged after the reaction. Referring to equation (1), this means an increase in v. This increase in v necessitates a change in k or in the concentration terms or in both. By hypothesis, the chemical equation is unchanged, therefore an increase in the value of k by the addition of a substance which does not appear in the products would denote a catalytic action, the temperature

remaining constant. The added substance, unchanged after the reaction, is the catalyst. Nothing is postulated with regard to the mechanism of the action of the catalyst.

Before going farther, it is necessary to consider the increase in the value of k more carefully. There are two ways in which this increase may appear. These two ways have not been considered separately heretofore as far as the writer is aware, but have always been used interchangeably in speaking of catalysis in general, although in the consideration of individual reactions at one time one way is specified, at another time, the other.

In the first place, the presence of a catalyst may increase the velocity of a chemical reaction by a definite amount. Thus, in the absence of the catalyst, k would have a certain constant value; in its presence, k would also be constant, but would be greater in magnitude. The new value of k would be as characteristic for the reaction with the given concentration of the catalyst, as the smaller value was for the reaction in the absence of the catalyst. Perhaps the best known example of this type of catalysis is the hydrolysis of sucrose in the presence of acids of different strengths, the rates being dependent within limits upon the concentrations of the hydrogen ions which are taken to act as catalysts.

In the second place, the presence of a catalyst in certain reactions causes an acceleration of the reaction; that is to say, with a certain amount of catalytic substance added initially, the velocity of the chemical transformation increases continuously. Numerous examples of this type of catalysis are known. Thus, the formation of ethyl acetacetate from ethyl acetate may be written as follows:

$$2CH_3CO.OC_2H_5 = CH_3CO.CH_2CO.OC_2H_5 + C_2H_5OH. \quad (3)$$

It was found that a very small amount of ethyl alcohol (or better sodium ethylate) was needed to have this reaction take place at an appreciable rate but that after it had started, the rate increased continually. The alcohol, or alcoxide, evidently acted as catalyst, and the alcohol formed as the reaction proceeded, itself then played a part as catalyst. The reason for the acceleration in this case is therefore to be ascribed to the continually increasing quantity of catalyst. It is well known,

of course, that the explanation commonly accepted for the mechanism of this reaction involves several successive steps. This will be referred to again later. Another set of reactions belonging to this class includes the hydrolysis of organic esters by acids not too highly ionized. Here, also, one of the products formed as the result of the reaction, acid in this case, acts as catalyst increasing the speed of the hydrolysis. A third reaction which may be mentioned is the action of permanganate on oxalic acid, a method for the quantitative estimation of the latter. The presence of a manganous salt increases the velocity of the reaction, and since in the reaction the manganese of the permanganate is transformed into such a salt, the amount of the latter continually increases and the reaction is constantly speeded up.

These two groups of velocity changes which are included under the Ostwald definition of catalysis can be differentiated sharply. The second group, including accelerated reactions in which the changes are connected with the behaviors of one or more of the products of the reactions exerting catalytic actions, have also been termed "auto-catalytic" reactions.

While the two types of velocity changes, finite increase and accelerated increase, can be differentiated sharply in any given experimental reaction, a closer analysis of the phenomena shows that fundamentally the same actions as regards the catalytic nature of the changes are involved. In the first case, the addition of a definite quantity of the catalytic substance to a reaction results in a certain increase in the velocity of the chemical change. The mechanism by means of which the catalyst causes this increase is not of special significance in the present discussion except that the catalyst must be involved in some way in the reaction. In the second case of accelerated change in velocity, or auto-catalysis, as the chemical reaction proceeds the substance which plays the part of catalyst is formed continuously as one of the products of the chemical change. The concentration of the catalyst therefore is continually increasing. The mechanism of the action of a definite amount of the catalyst in the second case may be considered to be similar to that of the mechanism of the action of the catalyst in the first case. Whatever explanation is adopted for one of the actions can be carried over to the other. There is no reason to consider the

mechanisms as different. The actual amount of change undergone in any small unit of time in either case will be dependent upon the concentration of the catalyst at that time. In the first case the concentration of the catalyst does not change throughout the reaction, in the second it is present in increasingly greater concentration as the reaction proceeds. The latter reaction might therefore be considered to be made up of a great number of separate reactions in each of which the concentration of the catalyst is greater than in the preceding reaction, but where each reaction strictly speaking may be classed as a reaction of the former type. The view of the whole series of reactions would give the reaction of the second type, that of accelerated change. The two types of reaction velocity increases are thus seen to be based fundamentally upon the same relations or changes, although experimentally they are readily grouped separately.

The definition of catalysis as involving an increase in the velocity of a chemical reaction is clear cut, and while perhaps limited in scope, gives a satisfactory basis for the classification of such reactions. Unfortunately, the definition did not remain as simple as this for any length of time. Ostwald, followed by Bredig, Stieglitz, and others, extended the view so that the change in velocity might be considered to be negative in sign as well as positive, or that catalysis includes retardation as well as increase. This negative phenomenon was termed negative catalysis. Innumerable examples might be given, and the reactions divided into groups as with catalysis; a definite decrease in velocity, and an accelerated decrease in velocity (negative auto-catalysis or auto-retardation). Examples of the former include the actions of certain organic substances (mannite, benzaldehyde, etc.) on the oxidation of sodium sulfite by oxygen,[1] the action of various substances in retarding the decomposition of hydrogen peroxide solutions, etc.; while a striking example of the latter is the action of the hydrobromic acid which is formed in the hydrolytic decomposition of bromopropionic acid on this decomposition.[2]

These negative catalysis phenomena have been explained

[1] S. L. Bigelow, *Z. physik. Chem.* *26*, 493 (1898).
[2] G. Senter, *J. Chem. Soc.* *95*, 1827 (1909); G. Senter and A. W. Porter, *J. Chem. Soc.* *99*, 1049 (1911).

most simply by the assumption of combination of the negative catalyst with one or more of the substances involved in the reaction, in this way decreasing its active concentration. Experimental evidence to support this view is available in a number of cases. This question will be developed farther in a later chapter.

Referring again to equation (1), the definition of catalysis would include the phenomena in which the value of k is changed (increased or decreased) by the presence of a substance which is itself unchanged as a result of the reaction. The change in k indicates a change in the velocity. By definition, this change may be negative as well as positive and is due to the presence of some substance which is unchanged as a result of the reaction (as shown in the chemical equation). This substance obviously must produce some action or be responsible for some phenomenon in the reaction, otherwise the velocity could not be increased or decreased. Now, since the change in velocity may be positive or negative because of some influence or action of the added substance, it may be asked whether the change in velocity might not conceivably be zero. That is to say, the effect of the catalyst would show itself in a velocity change ranging from positive, through zero, to negative. This change in velocity is a result of the action or influence of the catalyst. With zero change in velocity for certain reactions it is logically conceivable for a catalyst to be exerting an influence similar to that exerted in other reactions where the velocity is found to change. In other words, following the description of change in velocity as characteristic of catalysis one step farther, leads to the conclusion that there must be some underlying phenomenon responsible for the actions and that the change in velocity is only an accompanying phenomenon and dependent upon the former. A possible explanation of this underlying cause and a grouping of catalytic actions as part of a general classification and interpretation of chemical reactions will be presented in the following chapter.

It may be stated that as long as catalysis is assumed to include only an increase in reaction velocity the classification could be developed in a satisfactory manner, although only a narrow field would be covered. Extending the view to include

"negative" catalysis broadened the field, brought out many more analogies, but also showed that the definitions could not be adhered to strictly, since a consistent following out of the views led to conclusions indicating the necessity for a more fundamental definition of catalysis.

It was stated that the change in velocity of a chemical reaction by the presence of a substance which is unchanged at the end of the reaction would mean a change in k or in the concentrations of the reacting substances or in both. The chemical equation was assumed to be unchanged in the preceding discussions and the change localized in k. Some consideration may be devoted to the other possibility, a change in the concentrations of the reacting substances, especially since the experimental and theoretical studies of Stieglitz on catalysis have contributed much valuable material to this phase of the subject. His view, as already stated, is that "The one vital fact, then, of an acceleration due to an increase in the active mass or concentration of a reacting component in a catalytic action is the only fundamental fact common to all catalytic actions." It is this view, of increase in the concentration of reacting component, which is brought out so strikingly in Stieglitz's work, which it is desired to emphasize here, as it aids markedly in the development of the chemical explanation of catalysis, even if his views on acceleration as the dominating feature of catalysis are not followed.

Stieglitz [1] studied the mechanism of a number of hydrolytic and similar reactions whose rates of change were increased by the addition of acids. In place of following the changes occurring in the hydrolysis of esters, the decomposition of imido esters was first studied as furnishing more suitable experimental material. The decomposition of an imido ester, for example methyl imido benzoate, by water may take place as follows:

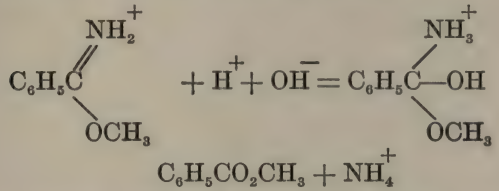
$$C_6H_5C(:NH)OCH_3 + H_2O = C_6H_5CO_2CH_3 + NH_3 \quad (4)$$

The addition of an acid such as hydrochloric acid was found to increase greatly the velocity of the decomposition of the imido ester. In this case the reaction was the following:

$$C_6H_5C(:\overset{+}{N}H_2)OCH_3 + H_2O = C_6H_5CO_2CH_3 + \overset{+}{N}H_4 \quad (5)$$

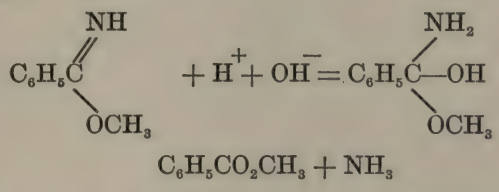
[1] The work was summarized in two papers: J. Stieglitz, *Jour. Amer. Chem. Soc.* **32**, 221 (1910); **35**, 1774 (1913).

The hydrochlorides, hydrobromides, and nitrates of imido esters were studied. Taking into account the degrees of ionization of the imido ester salts, and allowing for the salt effect (increased velocity), the reaction velocity agreed with the view that the reaction measured was the decomposition of the positive ester ion. The same rate of decomposition was found, irrespective of the salt from which it was derived, ". . . the simple reason why the addition of an acid accelerates this decomposition is that it forms a salt whose positive ion is the reacting component, and that the concentration of the ion is enormously increased when the catalyzing acid is added to the free ester, which is a very weak and therefore little ionized base." The reactions in all probability take place in stages as follows:



$$C_6H_5CO_2CH_3 + NH_4^+ \qquad (6)$$

in the presence of acids; and with water alone according to the equations



$$C_6H_5CO_2CH_3 + NH_3 \qquad (7)$$

It was pointed out that in all this work, the transformation in acid solution occurred in the sense that the positive ion of a weaker base was transformed into the positive ion of a stronger base. This fact will be referred to again in Chapter IV. Imido esters react with ammonia to form amidines. The rates of these reactions, also, were increased by the addition of acid, and the main reacting components were shown to be the positive ester ions. This reaction may be formulated as follows:

$$C_6H_5C(:NH_2^+)OCH_3 + NH_3 = C_6H_5C(:NH_2^+)NH_2 + CH_3OH \qquad (8)$$

Similarly, the rates of the reactions between urea esters and ammonia to form guanidines were increased by the addition of acid, the reacting components of the reactions which were being measured being the positive ester ions.

At the same time that the decomposition of the positive ion occurred in these reactions, water (or ammonia) acted on unionized ester but at a very much slower rate. For example, for the action between ammonia and methyl imido benzoate, the reaction involving the positive ester ion was about 50,000 times as rapid as that involving the unionized ester. At the same time, in observing the changes actually occurring, the unionized ester may be present in much greater concentration than the positive ester ion, so that experimentally the amounts of the two substances which will have reacted (or the amounts of the products formed in the two reactions) will be of the same order of magnitude, although their rates differed widely. These relations varied with the different reactions. With imido esters, the concentration of the positive ester ion in the presence of acid was comparatively large. At the other extreme is the reaction between acid ester and ammonia to form amide, as follows:

$$CH_3CO_2CH_3 + NH_3 = CH_3CONH_2 + CH_3OH \qquad (9)$$

This reaction is extremely slow, even in the presence of acids or ammonium salts, and is essentially a function of the ester and the ammonia. The relative concentrations of ester salt and therefore positive ester ion and uncombined ester in any one case depends upon the relative affinity of the ester and the other substances present for the acid. Thus, in the last case, the ester forming an extremely weak oxonium base can take only traces of acid from the ammonium chloride in the presence of ammonia. The ester salt is therefore present in very minute concentration and the molecular transformation, because of the larger concentration of reacting components, comes to the front experimentally. In the reaction between ester and water in the presence of acid to form organic acid and alcohol, the ester need compete for the acid only with an oxonium base of the same order of strength or perhaps rather weaker (oxonium base of water), and therefore the ionic reaction predominates. In any case, two simultaneous reactions are taking place. The actions of am-

monia on imido ester and on acid ester represent perhaps the extreme conditions. In the former, the action involves essentially the positive ester ion and the addition of catalyst (acid) would increase the velocity according to the mechanism outlined; in the latter, the action involves essentially unionized ester and the addition of acid to act as catalyst is ineffective for the reasons given.

The hydrolysis of esters and the reverse reactions of esterification in which the velocities of the actions are increased by acids assumes the formation of complex oxonium ion (ester or acid plus hydrogen ion of catalyst) as the chief reacting component. The kinetic relationships do not permit of a decision as to whether the acid or its derivative forms the oxonium salt and ion, or the alcohol or water. As a result of the imido ester studies, Stieglitz concluded that the first view was correct; that the complex ion involved the acid or its derivative. It may be noted that as a result of a series of extended studies including the retarding effects of small amounts of water either produced or added to the medium during the progress of esterification, Goldschmidt,[1] while coinciding in the view that complex salt formation occurs as an intermediate step in esterification and ester hydrolysis reactions, concluded that the alcohol or its derivatives formed the complex oxonium salt and ion.

The work of Stieglitz on imido esters and related compounds showed that the increase in concentration of positive ion because of the addition of highly ionized acid increased the rate of reaction. The highly ionized acid was therefore called the catalyst, but it was clearly shown that the increase in concentration of the positive ion accounted for the increased velocity. The changes in velocity in these cases may be referred to the changes in the concentrations of the reacting molecular species. It is evident that if the concentration terms refer to the total concentration of the imido ester (or similar) molecule, that the change in velocity would then vary with the different acids added. The acids would then be considered to be acting as catalysts, the concentrations would be unchanged, and the change in the velocity be reflected in the change of the value of k. The careful experi-

[1] H. Goldschmidt, *Z. Elektrochem.* **12**, 432 (1906); **15**, 4 (1909); *Z. physik. Chem.* **70**, 627 (1910); H. Goldschmidt and O. Udby, *Z. physik. Chem.* **60**, 728 (1907).

mental study of the reaction has however shown that the substance being transformed in the reaction was the same in every case (namely, the complex positive ion), that the acid added only changed the proportion of this positive ion, and that the actual chemical transformation of the imido ester ion was identical in every case. Inserting the proper concentration of positive ion into the kinetic equation would result in the corresponding value of k being unchanged. Until these relations had been worked out, the change in velocity would have been taken to be accompanied by a change in the constant k and the reaction termed catalytic in the sense that the action of the added acid was unknown except in so far as it increased the rate of reaction.

The problem appears to resolve itself into a question of definition. Under what conditions is a change in velocity to be referred to a difference in the nature of the chemical reaction? With regard to the imido ester reaction, the addition of different acids resulted in a different imido ester salt and different degree of ionization. The velocity being dependent upon the concentration of the ion might be different with different acids which had been added. The actual chemical change measured, that represented by the chemical equation as the change in imido ester, was the same in every case. At the same time, it cannot be denied that the reaction took place in steps; formation of imido ester salt, its ionization and the subsequent decomposition of the ester ion. The reaction measured kinetically was the last, the slowest of the series indicated. These steps were not indicated in the chemical equation, as apparently the added acid was unchanged as a result of the reaction. Strictly speaking, the complete chemical reaction was different in the different cases, and the velocity might therefore be expected to be different. At the same time, by choosing one of the stages of the reaction, it was possible to account for the increase in the velocity of the reaction by showing that the concentration of the reacting constituent (as against the total concentration of the indicated molecular compound) was changed under different conditions.

The example of the imido ester catalysis has been chosen as it is a particularly instructive one. As Stieglitz pointed out, it is representative of a number of reactions. It may be asked whether in other cases, where, in the kinetic considerations changes in velocity are observed, similar deductions would not be

permissible. The actions of catalysts, from the minute quantities involved in ester saponifications and similar reactions to the changes in solvents may show themselves in changing the velocity constants of the reactions. But the chemical equation which may be used to represent the change may represent only one of the stages of the reaction, and eliminating even the possibility of simultaneous or consecutive reactions being measured, a suitable change in the concentration of the reacting molecule or constituent frequently might account for the action of the so-called catalyst.

Chapter III.

Theory of Catalytic Actions.

The theory of reactions which is based upon the formation of addition compounds appears to offer the most satisfactory general viewpoint from which to consider the mechanism of chemical reactions. In the development of this theory it was found that by adding one simple concept and then basing the deductions upon well known laws and relations, a classification of catalytic actions was obtained which included and accounted for the views heretofore used in that field at the same time that the multiplicity of criteria suggested at various times was avoided.

The views on the theory of the mechanism of chemical reactions were presented in somewhat different connections in two recent publications by the writer [1] and the relations to a number of chemical phenomena developed. In this chapter an outline of the general theory of chemical reactions will be given briefly, to be followed by the consideration of catalytic reactions as a special group of chemical reactions, and finally some of the points of more direct interest in catalysis will be developed at greater length.

The addition theory of chemical reactions assumes that when two or more molecules react, they first combine to form an addition compound which then may or may not react farther to break down to form other products. Thus, for example, the reaction between an alcohol and an organic acid may be represented as follows:

$$\left[\begin{matrix} CH_3CO_2H \\ C_2H_5OH \end{matrix}\right] \begin{matrix} = C_2H_5OH + CH_3CO_2H & (a) \\ = CH_3CO_2C_2H_5 + H_2O & (b) \end{matrix} \qquad (1)$$

The method of writing the equations indicates the fact that the configuration of the intermediate compound, or the linkings of

[1] "Chemical Reactions; Their Theory and Mechanism." "The Chemistry of Enzyme Actions," Chapter III.

the atoms in it, is not definitely known. Also, it is not shown whether the reaction started with one set of products or the other; in other words, the factor of reversibility is brought out.

The obvious question which arises in connection with this reaction, and in fact, with all reactions, is whether the experimental evidence bears out this view of the mechanism of the reactions. The first point which must be made is that the addition (or intermediate) compound which is assumed to be formed appears in most cases not to be stable enough to be isolated and identified. The exact proportions of the different constituents present in it frequently cannot be given. At the same time definite evidence exists that such compounds are formed. If such addition compounds possess marked stability, the reaction is generally written differently and the chemical equation divided into several stages. This is true, for instance, for the Grignard reaction, where certain of the addition compounds have been isolated. Equation (1), for example, may be used in a more or less symbolical manner. There is considerable evidence at hand that in esterification as well as in the hydrolysis of esters, addition compounds are formed, but the composition of such compounds, whether containing two molecules of acid to one of alcohol, two of alcohol to one of acid, or whether or not containing water, is uncertain, and in fact may vary with the different alcohols and acids.

Equation (1) brings out certain additional relations. If none of the products or substances is removed from the reaction mixture, the concentrations of the various constituents present at equilibrium can be obtained if the equilibrium constants are known. Since the intermediate compound would appear in the mass action expressions of both reactions, one constant would be sufficient to determine the relative equilibrium concentrations. If equilibrium is not attained, or if one or more of the substances is removed from the sphere of action, then the actual composition of the mixture at any instant would depend upon the concentrations of the various substances and the velocity constants of the reactions. If the separate substances shown either in equation (a) or (b) were present initially, then the observed velocity would be made up of the velocities of the two separate reactions. If one of these takes place much more slowly than the other, it

would be the velocity of the slow reaction which would be observed experimentally.

Equation (1) represents a simple example of the explanation (partial, at any rate) of the mechanism of a chemical reaction. A number of such were given in another place.[1] It is evident that with more complex substances, or where three or more substances are taking part, more possibilities for the formation of different sets of products exist. Thus, several examples, which will be taken up again in connection with catalytic actions later in this chapter, may be quoted. The first of these is the reaction between ammonia, hydrogen chloride, and water, which may be written as follows:

$$\left[\begin{matrix}NH_3\\HCl\\H_2O\end{matrix}\right] \begin{matrix}= NH_3 + HCl + H_2O & (a)\\ = NH_4Cl + H_2O & (b)\\ = NH_4OH + HCl & (c)\\ = NH_3 + HCl.H_2O & (d)\end{matrix} \qquad (2)$$

An analogous reaction is that between ammonia, hydrogen chloride, and platinic chloride, which, omitting the possible participation of water, may be written as follows:

$$\left[\begin{matrix}2NH_3\\2HCl\\PtCl_4\end{matrix}\right] \begin{matrix}= 2NH_3 + 2HCl + PtCl_4 & (a)\\ = 2NH_4Cl + PtCl_4 & (b)\\ = (NH_3)_2PtCl_4 + 2HCl & (c)\\ = H_2PtCl_6 + 2NH_3 & (d)\end{matrix} \qquad (3)$$

As a development of reactions (1), esterification (or the reaction in which an alcohol and an organic acid take part) in the presence of an inorganic acid may be formulated in the following manner:

$$\left[\begin{matrix}C_2H_5OH\\CH_3CO_2H\\HCl\end{matrix}\right] \begin{matrix}= C_2H_5OH + CH_3CO_2H + HCl & (a)\\ = CH_3CO_2C_2H_5 + H_2O + HCl & (b)\\ = C_2H_5Cl + CH_3CO_2H + H_2O & (c)\end{matrix} \qquad (4)$$

It is obvious that in these formulations, all of the possible reactions have not been given. It would serve no useful purpose to elaborate the theory in this way in the present instance since

[1] "Chemical Reactions; Their Theory and Mechanism." Cf. also K. George Falk and J. M. Nelson, *Jour. Amer. Chem. Soc.* 37, 1732 (1915).

it is only desired to bring out the general principles in this connection. With more complex substances the possibilities would be greatly increased as far as the number of possible sets of products are concerned. The actual products observed in any case would depend on the relative velocities of the different reactions, the concentrations of the substances and their possible removal from the sphere of action if the mixture is not at equilibrium, and the relative chemical affinities as dependent on the free energy changes involved in the formation of the different sets of products, if the reaction mixture has attained a state of equilibrium.

A study of the chemical literature of recent years reveals the fact that as the study of the mechanism of chemical reactions is pursued more generally, an increasingly greater number of reactions is found to conform to the scheme outlined. It would lead too far here to quote different workers in this field, but the general trend of the views is apparent.

In place of starting with certain products which go to form an addition compound which may then decompose again into different products, it is possible to start with a more or less complex substance, or even in some cases a comparatively simple substance, which may decompose to form different sets of products, possibly depending upon the conditions used and the principle of mass action. A few examples of such reactions may be quoted, and, in order to include a somewhat different type, the reactions chosen will include oxidation-reduction changes.[1] A simple reaction of this type is given by the decomposition of formic acid.

$$\left[HCO_2H\right] \begin{matrix} = H_2O + CO & \text{(a)} \\ = H_2 + CO_2 & \text{(b)} \end{matrix} \qquad (5)$$

Water and carbon monoxide, reaction (a), are formed mainly when formic acid is heated with sulfuric or other mineral acids,[2] hydrogen and carbon dioxide mainly, reaction (b), by heating with platinum or with finely divided rhodium, ruthenium, or iridium.

The reverse of reactions (5) can also be carried out; that is, starting with the products on the right hand side of the equation, under suitable conditions formic acid will be formed.

With more complex bodies, the possibilities in the way of in-

[1] "Chemical Reactions; Their Theory and Mechanism," Chapter X.
[2] Cf. G. E. K. Branch, *Jour. Amer. Chem. Soc.* *37*, 2316 (1915).

creasing the numbers of sets of products will obviously be increased, but the general principles involved in determining the course of the reaction will remain the same.

Although the application of the addition theory to reactions of organic chemistry seems fairly simple in principle, it may appear as if more difficulty would be encountered in applying the same general views to reactions of inorganic chemistry, especially reactions taking place in aqueous and similar solutions, in which ions are involved. Some space may therefore be devoted to this question. According to the theory of electrolytic dissociation, reaction in solution takes place as a rule between ions and because of their presence. With the addition compound theory, reactions in solution are not assumed to take place because of the presence of ions. All combinations between atoms in molecules are assumed at the present time to be connected in one way or another with the transfer or sharing of electrons between or by the atoms. Combination is considered to be electrical in character. As pointed out by J. M. Nelson and the writer in various publications on the electron conception of valence and related subjects, a simpler and in many ways quite satisfactory theory of chemical combination can be developed by assuming a transfer of an electron in the production of every chemical linking. With regard to the relation between the extent of electrolytic dissociation and the occurrence of a chemical reaction ". . . the readiness or speed with which reactions occurred was a phenomenon not dependent upon the existence of ions. The occurrence, existence, and stability of ions in the same way had nothing to do directly with the occurrence of chemical reactions. There is, however, an indirect connection. The physical property shown by the ability to conduct the electric current in solution and the chemical property shown by the ability and readiness to undergo change in composition alone or in conjunction with other substances, are both assumed to be due to the same underlying cause. This cause, while producing both effects, need not produce both quantitatively at the same rate. That is to say, under certain conditions, the physical property would be much the more marked and amenable to experiment; under other conditions, the chemical . . . it is probable that in solution, the property of the solvent of forming addition compounds with the dissolved

substances is the common cause of the two sets of phenomena, physical and chemical. In aqueous solutions, compounds of the nature of hydrates, which have been shown to exist in a number of cases, may well be the cause. In some cases, such as with uni-univalent salts in aqueous solutions, very close parallelism exists between the physical and chemical properties, with uni-divalent and more complex salts, the parallelism is not obvious or does not exist at all. Quantitative proof of this theory is not at hand, but it has been found useful in the consideration of reactions and will be used here. To sum up these relations: The changes occurring in chemical reactions do not depend upon the electrolytic dissociation of the reacting substances. The chemical changes are accompanied very often by electrolytic dissociation phenomena, but the latter parallel the former (or vice versa) and do not necessarily precede or cause them. The electron conception of valence assumes the presence of excess electric charges on all atoms existing in states of combination, or the transfer of valence electrons when atoms combine. The experimental facts of electrolytic dissociation offer a method for making some of these electric charges susceptible to measurement, but electrolytic dissociation does not produce these charges on the ions due to valence combinations." [1]

The importance of the solvent in reactions taking place in solutions which show electrolytic dissociation is the feature which must be emphasized in considering such reactions from the point of view of addition compound formation. J. M. Nelson and the writer developed these views in various directions some years ago in a paper entitled "Electron Conception of Valence. VII. Theory of Electrolytic Dissociation and Chemical Action." [2] The most recent publication along certain of these lines is a paper by J. Kendall on "The Correlation of Compound Formation, Ionization and Solubility in Solutions. Outline of a Modified Ionization Theory." [3] Those interested in the more detailed exposition of these questions must be referred to the indicated publications, as it would lead too far to enter into greater detail in the present connection.

[1] "The Chemistry of Enzyme Actions," pp. 16-17.
[2] *Jour. Amer. Chem. Soc.* *37*, 1732 (1915).
[3] *Proc. Nat. Acad. Sci.* 7, 56 (1921); cf. also J. Kendall and P. M. Gross, *Jour. Amer. Chem. Soc.* *43*, 1416 (1921).

A definite viewpoint from which to consider the mechanism of chemical reactions has now been established. There is no intention of holding that it is the best which can be developed or that it is not subject to modification even in its present form. The fact which it is desired to emphasize is that the classification is a useful one in that it includes all chemical reactions without necessitating more or less arbitrary distinctions in the fundamental concepts. It is unfortunate that the quantitative evidence available at present to test the views advanced is not very extensive. The qualitative evidence appears to support them and it is to be hoped that the further quantitative work which is being carried on in various directions in connection with different phases of the general problem of chemical reactions will result in the acquisition of sufficient experimental data either to bear out the addition compound theory and to modify it if necessary, or to lay the foundations for a more satisfactory theory. For the present, it will be used as outlined in the preceding pages.

Catalytic actions form a group of chemical reactions and have been separated from other reactions in the past because of possessing certain characteristics. It was shown in the earlier chapters that the criteria which have been used for the purpose are not altogether satisfactory. In the publications by the present writer to which reference has already been made, a more definite classification of catalytic actions was attempted. This classification will be presented here, and also additional relations will be developed and an attempt made to indicate the significance of these relations in connection with some of the phenomena which have been observed with chemical reactions and their mechanism in general.

In considering catalytic reactions, the only limitation or definition which will be used is that in a chemical reaction, the chemical composition of one of the initial substances is the same as that of one of the products of the reaction. This criterion has been used in the past as one of the conditions which a catalytic reaction must follow, but there have always been other conditions which had to be obeyed. The difference in the views lies in the fact that unchanged composition of one constituent is the only factor which is defined in the present instance. All further

developments will follow from the general principles of chemistry and, especially in the consideration of the mechanisms of the reactions, the principles already given. It will be noted that changes in the velocities of reaction have not been spoken of in defining catalytic reactions. This omission differentiates the views developed here from those of Ostwald, Bredig, Stieglitz, and others. To the writer it appears as if the use of change in reaction velocity as the primary condition may lead to confusion, as already indicated. At the same time, change in reaction velocity will be considered in the proper place in connection with certain phenomena involved in catalysis.

The substance whose composition is the same before and after a chemical reaction in which it participates is called the catalyst according to the indicated view, and the presence of such a substance is obviously necessary for the reaction to be considered catalytic. The participation of a substance in a chemical reaction and its appearance unchanged in composition in the final products cannot readily be visualized unless the addition theory of chemical reactions, or some similar theory is used. To determine whether such a substance has taken part in the reaction, or in other words acted as a catalyst, evidently requires some change susceptible to experimental measurement. The most apparent changes which may be observed are in the first place, a change in the velocity of the observed reaction, and in the second place, the formation of different products in whole or in part. The isolation of addition compounds of which the assumed catalyst forms a part is valuable confirmatory evidence, especially if the addition compound itself can be shown to react further to produce the required products. These changes are secondary however to the original condition.

In order to illustrate and develop the relation in a more definite way, certain examples may be given.

Equations (2) already quoted earlier in this chapter form an instructive example and may be repeated here.

$$\left[\begin{matrix}\mathrm{NH_3}\\ \mathrm{HCl}\\ \mathrm{H_2O}\end{matrix}\right] \begin{matrix}= \mathrm{NH_3} + \mathrm{HCl} + \mathrm{H_2O} & \text{(a)}\\ = \mathrm{NH_4Cl} + \mathrm{H_2O} & \text{(b)}\\ = \mathrm{NH_4OH} + \mathrm{HCl} & \text{(c)}\\ = \mathrm{NH_3} + \mathrm{HCl.H_2O} & \text{(d)}\end{matrix} \qquad (2)$$

Ammonia and hydrogen chloride do not appear to react with appreciable velocity in the dry state. Addition of small amounts of moisture causes reaction to occur. With equations (a) and (b) (the addition compound is involved in both), water would be considered the catalyst. With reactions (a) and (c), hydrogen chloride might be considered the catalyst if this reaction occurred to an appreciable extent; with (a) and (d), ammonia might be considered the catalyst. The reaction observed in any given case depends upon the concentrations of the constituents, the relative velocities of the different reactions, the removal of one or more of the substances from the sphere of action, and the relative free energy changes of the different reactions as already outlined, depending upon whether or not the reactions have been allowed to come to equilibrium.

Equations (3) and (4) may be considered similarly and need not be repeated.

The question of change in reaction velocity on the basis of the suggested view of catalysis may be considered next. If the reaction between two substances to form two different substances takes place at a definite rate, then, if a catalyst is added, the course of the reactions may be symbolized in the following manner:—

$$\begin{array}{ll} [\mathrm{D}] = \mathrm{A} + \mathrm{B} & \text{(a)} \\ \quad\;\; = \mathrm{E} + \mathrm{F} & \text{(b)} \end{array} \qquad (6)$$

$$\begin{array}{ll} [\mathrm{H}] = \mathrm{A} + \mathrm{B} + \mathrm{C} & \text{(a)} \\ \quad\;\; = \mathrm{E} + \mathrm{F} + \mathrm{C} & \text{(b)} \\ \quad\;\; = \mathrm{M} + \mathrm{N} + \mathrm{C} & \text{(c)} \end{array} \qquad (7)$$

Equations (6) indicate the changes in the absence of catalyst; equations (7) the changes in the presence of the catalyst *C*. The products indicated, aside from the catalyst, by reactions (a) and (b) in both cases are the same; those in equation (c) are different.

Limiting the discussion for the present to the reactions (a) and (b), it will be seen that in comparing the rates of transformation of products (a) into products (b) in the two cases, three possibilities exist. Addition compounds, indicated by [D] and by [H] are formed in the two sets of reactions. In the first

set, equations (6), the addition compound is made up of the two reacting substances; in the second, equations (7), of the two reacting substances and catalyst substance. The combination of catalyst and one of the reacting substances obviously is also possible but will not be considered at this point since it only complicates the problem needlessly. Without the catalyst (equations (6)) the reaction proceeds at a definite rate. With the catalyst present the simultaneous formation of the two addition compounds shown in equations (6) and (7) is possible, and their decompositions evidently represent simultaneous reactions. If the velocity of the reaction involving the catalyst (equations (7a)-(7b)) is less than that of the reaction without the catalyst (equations (6)) (actually the sums of the velocities of the formation and decomposition of the additive compounds are meant), then, if there is a large difference, probably only a small part, if any, of the reaction will follow the former course, and the velocity will be practically the same in the two cases. As the difference between the rates becomes less, more of the reaction will involve the catalyst substance (equations (7)), and the total velocity observed may be smaller than in its absence, especially if the catalyst substance is present in considerable amount. If the velocities of the simultaneous reactions are the same, no change due to the catalyst would be observable. This represents the second possibility. For the third possibility, the reaction with the catalyst is the more rapid and will therefore be the reaction whose rate is being observed and measured. In considering these three possibilities, it is evident that the velocity of a chemical reaction will be observed to be diminished under special conditions because of the direct participation of a catalyst substance in the reaction. In most cases the velocity may be said either to be unchanged or increased. Only if there is a change would the velocity measurements give evidence for the presence of a catalyst. Since a decrease is comparatively infrequent, the reason is evident for the belief that velocity increase is the predominating factor in catalysis. The present point of view shows, however, that this increase is a consequence of catalytic action and is not the controlling feature. It is the phenomenon perhaps most readily observed as a result of catalytic action, but it represents only a single case in the way of possible changes.

The application of these views to the decomposition of imido esters and related compounds in the presence of acid in aqueous solution as studied by Stieglitz, which was described in some detail in Chapter II, is obvious. The simultaneous reactions there involve the decompositions of the unionized molecules and of the positive ester ions. The effects of the relative rates of the different reactions and of the relative concentrations of the reacting components were shown to be reflected in the relative amounts of the products formed in these simultaneous reactions.

In the consideration of the mechanism of chemical reactions, it was pointed out that the removal of certain products from the sphere of action would result in the reaction taking a certain course according to the principle of mass action. The removal of products may be brought about by mechanical means or by chemical reagents. In the latter case, such actions must not be confused with catalytic actions, but at the same time, the actions of catalysts must not be interpreted as being of such a nature. It is difficult at times to decide whether a given substance is acting solely as a catalyst, or also by the removal of certain products of reaction. Thus, the decomposition of formic acid as formulated in equations (2) may follow (a) in the presence of sulfuric acid perhaps because of the combination of the acid with the water, and (b) perhaps because of the combination of the platinum, rhodium, ruthenium, or iridium, with the hydrogen, but the conclusions are not certain and the possibility remains that the reactions are catalytic. In most cases, however, there is no room for doubt of this nature.

The phenomenon of negative catalysis, or retardation by catalysts, has been shown to be possible if the velocity of the reaction in the presence of the catalyst substance is less than in its absence with certain limitations as to the difference in these velocities and the amount of catalyst substance as already pointed out. Most of the phenomena which have been termed negative catalyses are due, however, to combination of the catalyst with one or more of the products of the reaction, or to the presence of so-called catalyst poisons which appear to act by combining with the catalyst and thus preventing its action.

The action of a catalyst may make itself apparent by causing the reaction to take a different course, as already stated and

as indicated in equations (7a) and (7c). These phenomena might be considered in the most general way to involve two possibilities. The reaction between two or more products tends to form an addition compound which may react further to form different sets of products (equations (7b) and (7c)) with velocities characteristic for each set under the given conditions. The participation of the catalyst substance in the make-up of the addition compound and the subsequent breaking down of the latter to form the same sets of products as in the first case plus catalyst substance, may very well, because of the presence of the catalyst substance, take place with quite different velocities. There may be a greater number of successive reactions in the presence of the catalyst. A different possibility of the action of the catalyst substance results if the view is taken that because of it the reactions are fundamentally different; that a different addition compound is formed, that the formation as well as the decomposition of the addition compound will be different because its constituents are different. Different sets of products, different velocities for the same sets of products plus catalyst, etc., might well be expected under these conditions. An example of this has already been given. In equations (1) and (4), the reaction between alcohol and acid in the absence and presence of a catalyst would give the same set of products as shown in (a) and (b) for both, but in the presence of the catalyst the additional possibility (c) is present, and is observed to a considerable extent if a tertiary alcohol is used.

The explanation of catalytic actions on the basis of one of the two preceding views is greatly a matter of personal inclination at present. In cases where sufficient experimental evidence is available there is, as a rule, no room for doubt. In other cases the matter is of minor importance and cannot be decided satisfactorily unless more data are at hand. This is illustrated by the examples which follow, in which different products are obtained depending upon the catalyst substances used.

The decomposition of formic acid as shown in equations (5) is an interesting example. A recent study [1] showed that formic acid vapor passed through a platinum tube at 1150° formed in the first instance hydrogen and carbon dioxide. These products

[1] J. A. Muller and E. Peytral, *Bull. soc. chim.* **29**, 34 (1921).

in some cases or under certain conditions reacted farther to form water and carbon monoxide, or the hydrogen reacted with formic acid to give hydrocarbons, but the primary reaction was the simple decomposition indicated. The direct formation of carbon monoxide and water by heating formic acid with sulfuric acid (and presumably with other mineral acids) was considered by these investigators to involve several steps, and not to be only a dehydrating action.

The decomposition of alcohol may give different products as follows:—

$$\left[\begin{array}{c} \\ 2C_2H_5OH \\ \\ \end{array}\right] \begin{array}{ll} = 2C_2H_4 + 2H_2O & \text{(a)} \\ = 2CH_3CHO + 2H_2 & \text{(b)} \\ = (C_2H_5)_2O + H_2O & \text{(c)} \end{array} \qquad (8)$$

The reaction may follow equation (a) or equation (b), or both, in the presence of different oxides; with thoria, very little of the reaction products shown in (b) are formed, with magnesia, very little of those shown in (a), while other oxides give results intermediate between these.[1] These reactions will be taken up again in Chapter VIII. The substances shown in equations (a) and (c) may be obtained by heating the alcohol with sulfuric acid; ethylene being formed preferably at one temperature, ether at another. Ether has also been obtained by heating the alcohol at higher temperatures with oxides such as alumina.

Ethyl acetacetate may decompose according to the following equations:—

$$\left[CH_3COCH_2CO_2C_2H_5\right] \begin{array}{ll} = CH_3COCH_3 + CO_2 + C_2H_5OH & \text{(a)} \\ = 2CH_3CO_2H + C_2H_5OH & \text{(b)} \end{array} \qquad (9)$$

Reaction (a), ketone decomposition, takes place on heating with dilute sulfuric acid or with dilute aqueous solution of alkali; reaction (b), acid decomposition, by heating with a concentrated solution of alcoholic alkali. Whether these reactions are to be classed as catalytic will depend upon the definition of catalysis which is adopted.

Chlorine and benzene react in sunlight to form addition com-

[1] P. Sabatier and A. Mailhe, *Ann. Chim. Phys.* (8) *20*, 289 (1910).

pounds; in the presence of iodine chloride both addition and substitution products are formed; and with stannic chloride or ferric chloride only the substitution products are obtained.[1]

With hydrazine, the following reactions have been found to occur:—[2]

$$\left[\begin{array}{c} \\ 6N_2H_4 \\ \\ \end{array}\right] \begin{array}{ll} = 8NH_3 + 2N_2 & \text{(a)} \\ = 6NH_3 + 3N_2 + 3H_2 & \text{(b)} \\ = 4NH_3 + 4N_2 + 6H_2 & \text{(c)} \end{array} \qquad (10)$$

Reaction (a) mainly occurs with hydrazine sulfate, reaction (b) with free hydrazine, and reaction (c) in the presence of alkali.

Many examples of oxidation and reduction of organic and also of inorganic compounds might be mentioned in this connection. The possibility of obtaining different products rests frequently upon the special reagent which is employed. It will hardly be necessary to give specific examples of such reactions. A number of them belong to the group of catalytic reactions. The use of various metals in many oxidations or reductions need only be mentioned.

A different group of reactions is included in the actions of different enzymes upon the same material giving different products. An interesting example which may be quoted involves the decomposition of the trisaccharide raffinose.[3] Sucrase (top yeast extract) hydrolyzed raffinose to form melibiose and fructose, while emulsin hydrolyzed raffinose to form sucrose and galactose.

These examples will serve to show the nature of these reactions and may also indicate problems which might profitably be studied.

The changes in reaction, either in the velocity or in the course, brought about by catalyst substances may be looked upon from a different point of view as changes in the environment which manifest themselves in the indicated manner. The catalyst substances bring about these changes in reaction in a definite way, one step being the formation of addition products. Changes in reaction can be brought about also by altering the physical con-

[1] A. Slator, *J. Chem. Soc. 83*, 729 (1903).
[2] S. Tanatar, *Z. physik. Chem. 40*, 475; *41*, 37 (1902).
[3] C. S. Hudson, *Jour. Amer. Chem. Soc. 36*, 1566 (1914).

ditions, by removing products of reaction, etc. Catalyst actions form therefore one of the ways in which different reactions may occur starting with the same substances. It is of interest to note that Berzelius looked upon catalysis from this point of view as shown by the quotation from his writings given on page 12 in considering changes in the body where from the same liquid (blood) in different parts different products may be formed.

Following directly from the considerations given, it is clear that very small amounts of substances can act as catalysts since the catalyst substance is formed again in the decomposition of the addition compound of which it forms a part. This fact has been used in the past as one of the criteria of catalytic actions, and it is also a direct outgrowth or development of the views outlined here. At the same time, the definition of catalyst is not limited to small amounts of substances according to these views. The amount does not come into question as far as the theoretical significance of the views is concerned. It may vary from infinitesimal amounts up to being the predominating substance present. The latter would be the case with many reactions taking place in aqueous solutions where the water would be considered to be the catalyst. At the same time, all of the water present would not be acting as catalyst all the time, but only that portion actually combined with the ions or molecules which are reacting.

This raises another question with regard to the action of the catalyst in considering, for example, possible changes in reaction velocities. With very small concentrations of catalyst substances and large amounts of other reacting materials, assuming no secondary reactions of the products with catalyst, etc., a definite fraction of the catalyst present would continually exist in combination in the addition compound and the remainder (possibly only a very small amount) would be present free in the reaction mixture. A steady state would exist, and under these conditions a definite constant change (increase) in velocity due to the catalyst would occur. With increasing quantities of catalyst, after a certain stage this steady state would no longer be probable, but the concentration of combined catalyst would change as the reaction proceeded, depending upon the relative concentrations of reacting substances and catalyst substance. This condition would

also occur with small amounts of catalyst after a great part of the initial substances had been transformed. Under these conditions the change in velocity due to the presence of the catalyst will not be constant but will change as the reaction proceeds because of the changes in relative concentrations of the reacting substances, including the catalyst.

The theory of catalytic actions as based upon the single criterion of one substance (identified as the catalyst) in a chemical reaction possessing the same composition after the reaction as before appears to be straightforward and direct and simple of application. It has been shown how a number of the phenomena ordinarily grouped under catalysis follow by the application of simple chemical principles, and the necessary limitations of the deductions which develop directly from these applications have also been pointed out. Further relations of similar nature will be presented in the succeeding chapters.

The remainder of this chapter will be devoted to the consideration of a difficulty encountered in the application of the views as outlined. The significance of the views is simple and not the cause of the difficulty; it is in the study of certain reactions which from one point of view are definitely catalytic but which do not conform to the strict definition as given. The fundamental difficulty lies in the fact that it is difficult to limit a reaction to one definite change. The products of a reaction may react farther, the catalyst substance from its very nature being far from inert, may participate in reactions with the products and cause complications, etc. In other words, in the experimental study of the reactions, the meaning to be ascribed to the words "same composition after the reaction as before" forms the crux of the difficulty. In the hydrolysis of sucrose or of esters by acid, in the combination of hydrogen and oxygen in the presence of platinum or palladium black, in the combination of ammonia and hydrogen chloride in the presence of water vapor, etc., this question does not arise. In the Friedel-Crafts reaction, the reaction is carried out experimentally in several stages in one of which the aluminium chloride, the catalyst, is decomposed intentionally. Here, in the classification, only the first part of the reaction would be considered catalytic, but even here the possibility exists that the aluminium chloride is com-

bined with a product of the reaction. In the hydrolysis of an ester by a base such as sodium hydroxide, according to the equation

$$RCO_2R' + Na^+ + OH^- = RCO_2^- + Na^+ + R'OH, \quad (11)$$

omitting the part played by the solvent water, there is no reason to consider the hydroxyl ion as the catalyst. The Na^+ ion, according to equation (11) would be the catalyst. This is contrary to experiment, however, since it is found that the reaction is due to the OH^- ion and not to the Na^+ ion. The more nearly correct equation would be

$$RCO_2R' + OH^- = RCO_2^- + R'OH \quad (12)$$

omitting the possible action of the solvent again. This reaction would therefore, strictly speaking, not be classed as catalytic.

The catalytic decomposition of imido esters as studied by J. Stieglitz and his co-workers to which extended reference was made in the last chapter, may be referred to again in this connection. The reaction velocity is increased by the addition of acid (hydrochloric acid, for example) but in the final products ammonium chloride is present. The question as to the exact catalyst is pertinent. Stieglitz showed that the increased velocity was due to the increase in concentration of the constituents (ions or molecules) which reacted. Hydrochloric acid increased the concentration of the reacting ion by forming a highly ionized salt. Hydrochloric acid was added as such but in the reaction mixture was present combined in the imido ester salt. The reaction studied took place in a number of stages which were investigated separately. According to the definition used here and interpreted strictly, hydrochloric acid would not be considered the catalyst in this reaction.

This raises at once another pertinent question. If the careful study of such a reaction as the imido ester hydrolysis has interpreted in a satisfactory way the mechanism of this reaction without introducing conceptions not already included in chemical theory, is there any reason to class this reaction as catalytic. From the point of view developed here, there would be none. Stieglitz considered change in reaction velocity as the

only characteristic property of catalytic reactions, but as shown in Chapter II, this definition is not satisfactory for a general classification. The conclusion seems to be unavoidable that a careful study of many reactions classed as catalytic at the present time, would make it possible to account for the mechanisms of these reactions in definite chemical ways. The question of unchanged composition of a catalyst may perhaps be best answered by considering the catalyst substance as a component of the reaction mixture in the sense that component is used in phase rule discussions. There is, however, a real difficulty here which may be solved by the introduction of a suitable definition for "unchanged composition." Perhaps the further consideration and treatment of catalytic reactions from the point of view advocated here will bring definiteness to the relations and show the most satisfactory meaning of the term to be adopted.

Chapter IV.

Energy Relations.

In the treatment of catalytic actions, a change in reaction velocity has generally been looked upon as one of the most striking and characteristic features of such actions and has frequently been used as the chief criterion. It was pointed out in Chapter II that a change in reaction velocity as the basic definition of catalysis was not altogether satisfactory. In Chapter III a different definition of catalysis was outlined. It was shown that this latter view brought out the reasons for the significance and importance ascribed to changes in reaction velocity with catalytic reactions, or perhaps better, with reactions which were grouped under the term catalytic by more or less common consent. Change in reaction velocity is a definite sign or symptom of catalytic change. It is a very important sign, but not the only one. It is secondary to the more fundamental phenomenon which really characterizes catalytic actions and which was discussed in some detail in the preceding chapter.

The consideration of the mechanism of a chemical reaction, including its velocity, raises the question of the reaction in the reverse direction. All chemical reactions are reversible theoretically, many are so practically. The reversibility of a chemical reaction and its connection with reaction velocity leads directly to the concept of equilibrium conditions of the reaction. This can be shown readily by means of the following equations:

$$v_1 = k_1 c_1 c_2 \ldots\ldots \qquad v_2 = k_2 c'_1 c'_2 \ldots\ldots \tag{1}$$

If $$v_1 = v_2 \tag{2}$$

Then $$\frac{k_1}{k_2} = \frac{c'_1 c'_2 \ldots}{c_1 c_2 \ldots} \tag{3}$$

Denoting $\frac{k_1}{k_2}$ by K, then

$$\frac{c'_1 c'_2 \cdots}{c_1 c_2 \cdots} = K \qquad (4)$$

At equilibrium, the velocity of the reaction in one direction is equal to the velocity in the opposite direction (equation (2)). Under this condition the composition of the mixture would remain unchanged. The concentrations of the various substances present would then be given by equations (3) or (4). The constant K is the well-known equilibrium constant whose value is determined by the mass action law. As deduced, K is shown to be constant at constant temperature and pressure. The limitations inherent in the velocity equations are to be found in the equilibrium expression as well. Thus, the c terms represent concentrations, and the equation is really an expression of the law of concentration action, and not directly of mass action, as already indicated in Chapter II. The equations as deduced are true only for dilute solutions and for gases at not too great pressures.

The equation for the equilibrium constant can also be deduced on purely thermodynamic considerations. This is done with the aid of the conception of the equilibrium box (van't Hoff). This deduction involves the assumption of the validity of the simple gas laws and is therefore also limited to dilute solutions or to gases at moderate pressures.

In the development of the thermodynamic treatment of chemical reactions, the equilibrium constants of chemical mixtures are connected with certain energy relationships. Thermodynamics does not involve a time function and consequently the theoretical developments based upon thermodynamics alone cannot directly involve such a relation as reaction velocity. As will be shown in Chapter V, it is necessary to bring in some different viewpoint such as the treatment based upon statistical mechanics to include the conception of time as required in the reaction velocity relationships. Catalysis has frequently been assumed heretofore to involve a change in reaction velocity, and thermodynamics is not applicable directly to reaction velocities. There does not therefore appear to be any point of direct contact be-

tween catalysis and thermodynamics at first sight. However, some relations have been developed in the past, which, although in a sense negative in character, are of fundamental interest. Also, it is possible that if a more general or less limited definition of catalysis is accepted, further applications of thermodynamics to catalytic reactions may be expected.

The first question which may be taken up is the influence of the catalyst on the equilibrium constant, and, since the equilibrium constant may be considered to be made up of the velocity constants of the two opposing reactions, on these velocity constants, or on the velocities of these reactions. The discussions in the past have been centered mainly upon certain definitions which have been proposed and from which definite deductions were made. The first important property of a catalyst which has been accepted widely is that it increases the velocity of a chemical reaction, the second that it is itself unchanged as a result of the reaction. Now, van't Hoff showed that if the catalyst is unchanged as a result of the reaction, the equilibrium of the reaction must be the same, whether or not the catalyst is present, since otherwise energy could be obtained from the reaction without introducing it in any way. Analyzing this view a little more carefully, it is evident that the crux of the question is to be found in the significance of the statement that the catalyst is unchanged in the reaction. It is the same question which was discussed at the end of Chapter III in considering the definition of catalytic actions. From the point of view of the equilibrium expression (equation (4)), it may be taken to signify that the concentration term c representing the catalyst is the same in the numerator and in the denominator of the fraction, or the same for the initial and the final states of the reaction mixture. Under these conditions the value of K will be the same in the presence and absence of the catalyst, and the change in free energy (or the chemical affinity) of the reaction will be identical whether or not the catalyst is present.

This conclusion is definite and clean-cut, but in the application to chemical reactions, it is soon evident that it represents a set of conditions limited to a more or less ideal case. The chemical equation representing a chemical reaction is, as a rule, definite in that a specific change or reaction is illustrated. The

mathematical equations involve deductions from the chemical equation by the application of mathematical processes to terms which represent to a greater or less degree of approximation the chemical terms or substances in the chemical equation. In these equations, first chemical and then mathematical, the changes considered are perfectly definite. In the actual chemical reaction, the conditions are hardly ever such that the chemical and mathematical equations denote the complete condition of affairs. Generally more than one change is possible in the chemical reaction and the chemical equation may represent only the change in which the worker is interested. Other changes which may occur are ignored. Also, substances which take part, but whose final composition is the same as their initial composition, and which apparently are not involved, are not, as a rule, included in the chemical equation. Solvents and their actions are frequently omitted. From the definition of catalysts used here, it can be seen that they also would frequently not be included in the chemical equations.

The three concepts, chemical reaction, chemical equation, and mathematical equation, are supposed to describe the same phenomenon in any given case. Actually they do so only as an ideal condition, and the possibility of deviation becomes greater with increasing complexity of the reactions and with decreasing care in the use of terms and expressions. To develop these views somewhat farther it is evident that the composition of a chemical constituent in a reaction mixture might be unchanged as the result of a reaction but that it might be in combination with one or another constituent in that mixture. For example, the action of an acid such as hydrochloric acid in aqueous solution hydrolyzing an ester such as methyl acetate, would as a rule be classed as catalytic. The question then comes up, if the catalyst is to be represented in the mathematical expression (equation (1)) what concentration should be used. For a time the concentration of the molecular hydrogen chloride (HCl) was used. More recently the hydrogen ion (H^+) has been assumed to be the catalyst. However it is known that the hydrogen ion in aqueous solution is hydrated and the term representing the concentration of this particular molecular species should have the form $(H.(H_2O)^x)^+$. In the presence of an ester the matter is complicated still farther

as the hydrogen ion may also be in combination with it to a certain extent. After the hydrolysis reaction has gone on for a time, the presence of alcohol and organic acid with their possibilities of combination with the hydrogen ion (or possibly hydrogen chloride molecule) adds to the complications. It would then be difficult to determine the concentration term in the mathematical expression which would contain the hydrogen chloride or hydrogen ion. Probably several would contain it. It follows therefore that whether the hydrogen and chlorine would still be considered to be associated with each other as hydrogen chloride, or, in aqueous solution as hydrochloric acid, and producing hydrogen ions in the latter case, the use of a simple concentration term in the mathematical equation to represent this substance is open to question. Similar relations hold for practically all catalytic reactions taking place in aqueous solutions and probably for many reactions in non-aqueous solvents. For reactions in gaseous systems, similar relations hold. In the catalysis of the reaction between ammonia and hydrogen chloride by water vapor, it can readily be seen that the water vapor may, to an increasingly greater degree, be combined with the ammonium chloride formed, as the reaction proceeds. In the reactions included under contact catalysis, which will be considered more in detail in Chapter VIII, the relations do not appear to be so simple, but if each reaction of this type is considered independently, it will be possible to determine to what extent, if any, the state of combination of the catalyst has changed during the reaction.

A comparison of the chemical reaction, chemical equation, and mathematical equation, will throw light on many of the questionable points involved. Each of these concepts has been evolved on certain definite bases, and each possesses certain limitations. The treatment of successive reactions also serves to illustrate this question. The use of a chemical equation to represent one or more of the steps of a series of successive reactions is greatly a matter of choice or convenience and the mathematical equation will then, in addition to the limitations inherent in its nature, also contain the limitations included in the application of the chemical equation to the chemical reaction. The chemical and mathematical equations may then furnish only an approximate and

one-sided picture of the chemical reaction which is being considered. These views, applicable to chemical reactions in general, will bring out the weaknesses of the classification of a group of reactions such as catalytic reactions. The difficulty of defining in a completely satisfactory manner the properties of such a group of reactions is striking. Reactions which may or may not be assigned to the group will be found as soon as a definition, more or less rigid, is suggested. This, again, raises the question as to the permanent value of a grouping such as that involved in catalysis. It may be repeated, without making a definite statement as to its permanent value at the present time, that the grouping has been of value in calling attention to the unknown mechanism of these reactions and the probable relations to reactions in general.

To return to the question of state of combination of the catalyst, it is seen that in catalytic reactions, even if the catalyst is apparently unchanged, it will not always be possible to use the same concentration term for it in the concentration law equation for the initial and final products of the reaction. The chemical equation as ordinarily written is incomplete in that it does not show the action of the solvent for reactions taking place in solutions, the action of so-called "adsorption" for reactions taking place in two phased systems, etc. The general conclusion arrived at then is that, unless the catalyst is entirely uncombined, or is combined in the same way before and after the reaction has taken place, the equilibrium constant of the reaction may not be the same in the presence and absence of the catalyst. In the ideal limiting case of no combination or combination to the same extent, the equilibrium of the reaction will not be changed by the presence of the catalyst substance.

The same conclusion has been arrived at by a number of workers by considering energy relationships of catalytic reactions. Among these may be quoted G. Bredig,[1] who stated that if a catalyst is changed in a physical or chemical manner in the catalyzed reaction, the equilibrium of the reaction would not be independent of the catalyst, but would be dependent upon its nature and amount. A change in the vapor pressure of the catalyst necessitates a difference in the work required to remove

[1] *Ergebnisse der Physiologie 1*, 139 (1902).

the catalyst from the reaction mixture. As long as the amount of this work is the same under the same conditions before and after the reaction, the equilibrium would remain unchanged. If the catalyst is present in large excess it would act as solvent. A change in the nature of the solvent changes the equilibrium and only in dilute solution would the equilibrium here remain the same. These statements were repeated in somewhat different forms by various workers and some further points added and clarified without being adopted, however, in the general literature of catalytic actions.[1] Among those who have brought out views similar to those of Bredig may be mentioned E. Abel,[2] who stated, assuming the formation of intermediate products with the catalyst, that if the catalyst was in a different chemical or physical state at the end of the reaction from what it was at the beginning, it had given up or received energy, and that consequently a change in the equilibrium was conceivable; J. Stieglitz,[3] who pointed out the conditions under which the equilibrium of a catalyzed reaction would be changed; M. A. Rosanoff,[4] who spoke of the possibility of a catalyst influencing the equilibrium, and that it did not do so only when the molecular state of the reagents was not affected by the catalyst; W. D. Bancroft,[5] and a number of others.

It would be possible to describe a number of catalytic reactions in which the equilibrium has been changed as well as not changed by the catalyst. It would lead too far, however, to do this in the present connection. Reference to the larger text books and compilations of catalytic reactions must suffice. The main point is that the equilibrium may be changed by the presence of the catalyst if the views regarding catalysis as developed here are adopted. If, by definition, a catalyst can not change the equilibrium of a reaction, then a discussion of the question is unnecessary.

The application of these considerations to the velocities of catalytic reactions is simple in principle. As stated, the equilibrium constant is taken to be made up of the two velocity con-

[1] Cf. for example E. K. Rideal and H. S. Taylor, "Catalysis in Theory and Practice," 1919, pp. 18-23.
[2] *Z. Elektrochem. 13*, 555 (1907).
[3] *Am. Chem. J. 39*, 56 (1908).
[4] *Jour. Amer. Chem. Soc. 35*, 173 (1913).
[5] *Jour. Physic. Chem. 21*, 573 (1917).

stants of the opposing reactions. If the equilibrium of a reaction is unchanged by the addition of a catalyst, and if the catalyst increases the velocity of the reaction in one direction, then it must to a corresponding degree, act as a catalyst for the opposing reaction and increase its velocity. This deduction was made a number of years ago, and the general qualitative statement has been found to be true, although quantitative results to test this point are not at hand in sufficient amount for satisfactory conclusions to be reached. If, however, the equilibrium of a reaction is changed by the presence of a catalyst, then the velocities of the opposing reactions need not be affected by the catalyst to the same extent, and it is readily conceivable that the velocity of a reaction in one direction might be increased, while that of the reaction in the opposite direction not be affected at all. This may be tantamount to saying that the catalyst for the one reaction did not act as a catalyst for the opposing reaction, and from the preceding discussion might be explained chemically by considering that the catalyst substance was combined with some substance in the reaction mixture which prevented it from taking part in the desired reaction.

This view brings with it a chemical significance of catalytic reactions (as well as of other phenomena) which has been mentioned several times, but whose importance cannot be over-emphasized. The point which it is desired to make again in this connection is the importance which certain definitions may acquire, and which sometimes obscure the relations which are being studied. If these definitions are accepted, certain conclusions follow (such as the velocities of opposing reactions being increased by the catalyst if the equilibrium of the reaction is unchanged by it). On the basis of some other definition, different conclusions might be obtained, and in making positive statements with regard to the behavior of catalysts, it is always advisable to examine the postulates carefully.

The criteria of catalytic actions which were gradually evolved in the course of a number of years do not appear to the writer to be altogether satisfactory. It is for this reason that an attempt is being made to formulate a simpler definition, including, as far as possible, the relations heretofore developed, at the same time

showing the bearing on chemical phenomena not included in catalysis.

Another point may be spoken of in this connection. The question is often raised whether a catalyst can start a reaction or can only modify its velocity. This again can be looked upon as a matter of definition. If, by definition, a catalyst is a substance which changes the velocity of a reaction, then there seems to be no reason for considering that it can start a reaction, especially if, as is frequently the case, the proviso is added that it cannot change the equilibrium. If the definition states that the catalyst takes part and is unchanged in composition after the reaction, then, if the reaction products are the same in the absence and in the presence of the catalyst, the catalyst does not start the reaction. If, however, the products are different in part or altogether in the presence of the catalyst, then the reaction has evidently taken a different course to some extent, at any rate, due to the presence of the catalyst, and in this sense the catalyst has started the reaction. The question is an academic one, only included for the sake of completeness, and can be answered readily in any given case by stating the exact definition of catalysis which is being used.

In the discussion so far, the different theories of chemical action which have been suggested or used with catalytic reactions have not been taken up in detail. For instance, the catalytic actions of hydrogen ions or acids in aqueous solutions on the hydrolysis of sucrose or of esters has not been discussed or the different theories, such as the hydrogen ion view, the dual catalysis view, and the addition compound view, given. These phenomena represent more or less special cases, and since they have been treated by a number of workers from various points of view, will not be considered farther here. Reference only will be made to a brief discussion by the writer [1] of the views in connection with such actions of acids in aqueous solutions.

Catalytic reactions form a group of chemical reactions distinguished from other reactions by certain more or less marked properties or peculiarities. The exact nature of these properties is to a great extent a matter of definition, and many of the apparent contradictions and exceptions found in the various treat-

[1] "The Chemistry of Enzyme Actions," pp. 48-53.

ments of catalytic reactions have their cause either in a lack of understanding of the definition used, or an attempt to modify the definition by adding thereto in place of redefining the original viewpoint. In any event, no matter what definition or classification is used for the group of catalytic reactions, the fact remains that the general principles of chemical reactions and their energy relations must hold for them as for all reactions. Thus, a reaction which proceeds isothermally and at constant volume will form products in which the free energy of the reaction mixture is decreased. This decrease in free energy does not involve directly the question of rate of reaction and according to the older viewpoints would not be included in a discussion of catalytic actions. At the same time, some experimental studies have been carried out which are of interest in connection with the possibility of linking up affinity relationships, reaction velocities and changes in these by suitable catalysts, and structural chemistry.

The work of Stieglitz on the decomposition of imido esters and related substances and the increase in their rates of decomposition by the addition of acids which was described in Chapter II may be referred to again in this connection.[1] The striking observation was made that in all the reactions studied, the catalytic action of the acid was found to be intimately connected with the transformation in acid solution of the positive ion of a weaker base into that of a stronger one "the results no doubt of the principle of the loss of a maximum amount of free energy." It was found to be a general rule in these changes that the transformation "proceeds with the greater velocity at a given temperature the weaker the original base is."

A few of the reactions studied by Stieglitz may be quoted in order to show the significance of these relations and their importance in accounting for the action of the catalyst in some cases, and lack of action in others. Imido esters are rapidly decomposed by water in the presence of acid, because the ammonium hydroxide which is the base corresponding to the ammonium ion formed in the reaction is a stronger base than the imido ester base. On the other hand, urea ester salts are quite stable in water in the presence of acid. The urea ester base is a stronger base than ammonium hydroxide, the opposite relation to the

[1] J. Stieglitz, *Jour. Amer. Chem. Soc.* **32**, 221 (1910).

first example. If instead of a urea ester, a benzoyl urea ester, which forms a weaker base than ammonium hydroxide, is used, the decomposition proceeds smoothly in the presence of acid. Similar relations were found to hold with the action of ammonia (or ammonium salts) on these substances in place of water, the positive ion of the weaker base being transformed into the positive ion of a stronger base. Thus, imido ester salts reacted with ammonia in the presence of acid (or with ammonium salts) to form amidines (stronger bases than imido esters); urea ester salts reacted with ammonia to form guanidines, in contradistinction to their lack of action with water, since urea ester bases are stronger bases than ammonium hydroxide, but weaker bases than those derived from guanidines, etc.

The conclusions of Stieglitz mark a definite attempt to bring catalytic actions into line with other chemical reactions in suggesting the change in free energy as a classifying principle. Unfortunately, data are not as yet available for reactions such as have been described, for the free energy to be calculated. Unquestionably, in the course of time, with the work on chemical equilibria and free energy or chemical affinity measurements which is in progress, the gaps in the knowledge of such relations will be filled in and a true measure of the affinity changes obtained. It may be recalled that a beginning has been made in such studies by C. G. Derick [1] in following rearrangements of the non-reversible type, of compounds which spontaneously go over into a more stable state. An example of this may be quoted in the rearrangement of $\Delta^{2,5}$-dihydroterephthalic acid to the $\Delta^{1,5}$ isomer. Heating caused this reaction to go to completion in a short time, while the $\Delta^{1,5}$ acid rearranged to the $\Delta^{1,4}$ acid when boiled in the presence of hydroxyl ions. A number of similar examples were given. These rearrangements took place slowly in the absence of a catalyst (heat apparently may be taken to produce the same effect as a catalyst). It was pointed out that the criterion of stability in such rearrangements may be taken to be the logarithm of the ionization constants of such substances acting as acids and bases. This can be deduced from the free

[1] *Jour. Amer. Chem. Soc.* **32**, 1333 (1910).

energy expression (of the second law of thermodynamics)

$$A = RT\log_e K, \tag{5}$$

in which K is the ionization constant and A the free energy of ionization, or the change in free energy "as expressed by the reaction $HA \rightleftarrows H^+ + A^-$ for acids and $ROH \rightleftarrows R^+ + OH^-$ for bases when the initial and final substances are at unit concentration. Therefore, the above expression gives a measure of the free energy of ionization in terms of the ionization constant and shows that the free energy of ionization is directly proportional to the natural logarithm of the ionization constant. Since that acid is most stable toward ionization which possesses the smallest amount of free energy of ionization, it is evident that when one acid has a smaller ionization constant than another, the change in free energy of ionization is smaller and its stability with respect to ionization is greater." The result of the comparison of the ionization constants of a number of the isomeric acids showed that "the free energy of ionization of the initial substance is greater than that of the final substance and that during the rearrangement there has been a decrease in free energy. . . . The final (stable) substance in a series of true rearrangements of the non-reversible type has a smaller ionization constant (or free energy of ionization) and the logarithm of the ionization constant may therefore be taken as a criterion of stability in these rearrangements."

This work of Derick is quoted for another reason. The ionization constants of the acids decrease as they rearrange to the more stable forms. In Stieglitz's work with imido esters and analogous compounds, there was a definite tendency for the reactions to take place in the sense that salts of stronger or more highly ionized bases were formed. Stieglitz, however, was not in a position to calculate the changes in free energy in these reactions. Both sets of conclusions are based upon reliable experimental work and cannot therefore be questioned. The degrees of ionization of the salts of the acids and bases in the two series of experiments do not enter into the considerations. The obvious conclusion is reached that there is no general relation with regard to ionization constants and stability in determining the course of a reaction. Each reaction studied, and the exact equilibrium con-

ditions under which it is investigated, must be considered independently, and conclusions obtained with one series of reactions cannot be carried over to another in a superficial manner. The one fundamental relation will hold, that in every case, a decrease in free energy will occur, if the reaction proceeds isothermally and at constant volume.

The relation of such work to catalytic reactions will become clearer in the future as the knowledge increases concerning the mechanism of such reactions, their equilibrium conditions, the free energy changes derived from these, and the factors governing the rate of attainment of equilibrium and the actions of various substances on the mechanism and rate.

Before leaving the work of Stieglitz on imido esters, reference may be made to a point to which attention was already directed in previous discussions. In the decomposition of imido ester with water, the unionized imido ester molecule was shown to be undergoing change; in acid solution, it was mainly the positive imido ester complex ion which reacted. The latter reaction was much more rapid than the former, and the increased speed was ascribed to the catalytic action of the added acid (or hydrogen ion). As stated previously, Stieglitz pointed out that in acid solution, the unionized molecule reacted as well as the positive ion, that the concentration of the latter might be much smaller than that of the former, and that consequently both reactions could be observed experimentally simultaneously. In fact, he showed that by suitably modifying the substances he could vary the extents of the two reactions taking place. The part played by the acid (or hydrogen ion) in the reaction was perfectly definite in increasing the concentration of the positive imido ester complex ion.

The point to which it is desired to call attention again is whether the catalyzed and uncatalyzed reactions may be considered to be the same in the sense that a reaction whose velocity is increased by a catalyst is generally considered to be unchanged in nature. The thorough study of the reaction in which an imido ester is decomposed under several different conditions has shown the probable mechanism of the reaction in the different cases. The significance of the term catalyst as used in the older (as well as in much of the newer) literature seems to

be indefinite. The acid plays a definite part in the decomposition of the imido ester, and in one sense it is present at the end (combined with a different grouping). The mechanisms of the reactions in the presence and absence of the catalyst are quite different. This is a striking example of the apparent lack of need for the conception of catalyst. Careful study showed exactly the part that the so-called catalyst played, and without using the conception of catalyst and treating the reaction as an ordinary chemical reaction, ignoring any specific virtue or harm which might be ascribed to the so-called catalyst, but honestly admitting ignorance where ignorance exists, it appears as if the knowledge of the changes involved would be just as satisfactory as when more or less imaginary and artificial concepts are invoked.

Chapter V.

Recent Theories of Chemical Action

The development in recent years of the views on the structure of matter will modify profoundly many of the present concepts of science. It is to be expected that some of these theories, for example those involving the structures of atoms and molecules, will be of special importance to chemistry, and will result in bringing to light many new phenomena and will account for many relations heretofore unexplained or explained unsatisfactorily. It is true that these newer theories have not as yet taken firm foothold in chemistry. The attempts to apply electronic structures to molecules, or to use radiation phenomena in chemistry, have been more or less isolated, but there can be no question that in comparatively few years these fundamental relations will be accepted and applied, perhaps in somewhat modified forms, to chemical phenomena. Chemical reactions and their mechanisms offer an inviting field for the application of some of these views. Certain theories in connection with them have already been developed, and it is for this reason that space will be devoted here to an attempt to outline some of these developments. Catalytic actions as a group of chemical reactions would naturally be considered at the same time. There is a further reason, however, for including catalytic actions in these discussions. It is possible that the views on radiation and related phenomena which are coming to the front will furnish a new and satisfactory explanation for many of the relations heretofore included under catalysis and in this way do away with the more or less incomplete definitions and classifications which have been proposed. The newer views and concepts are not final in any sense nor have they been generally adopted or accepted in chemistry even where applied. The fundamental theories appear to be sound, and it is quite certain that the developments from these will be of value ultimately, even if the

suggestions which have already been made and some of which will be presented here, should prove not to be the most satisfactory.

The fact that the velocity of a monomolecular reaction is finite can only signify, and this has been pointed out repeatedly, that the molecules of the substance undergoing change are not all in the same condition. For example, in speaking of the rate of decomposition of arsine, van't Hoff stated: [1] ". . . the slow progress of such a monomolecular reaction shows that not all the molecules of a gas are in the same condition, else either none would be decomposed or all together." In a reaction of higher order where two or more molecules react, the rate of reaction will evidently be dependent upon the frequency of the collisions or meetings of the molecules which are changed. Such meetings are not sufficient in themselves for reaction to occur. In addition, the molecules must be in the necessary state or condition as with a monomolecular reaction. There is possibly another factor to be considered, namely, the "steric" factor, according to which it is necessary for certain portions of molecules to meet in order to have the possibility of the occurrence of a reaction. This will be considered again later.

The fact that the velocity of a reaction of the second or higher order is not alone dependent on the number of meetings of the molecules can be shown most directly by the effect of increase of temperature. The kinetic theory of gases requires that for a rise of 10° in the neighborhood of the ordinary temperatures the number of collisions per unit of time increase about two per cent.[2] Experimentally, it has been found that the velocities of many chemical reactions are increased as much as two to three fold (200 to 300 per cent) by 10° rise in temperature. It is evident, therefore, that the kinetic theory alone does not account for the increase in reaction velocity with temperature. Similarly, other physical effects, such as viscosity, are insufficient as explanations. There must be involved some more deep-seated change within the molecules, as is indicated in monomolecular reactions.

[1] "Lectures on Theoretical and Physical Chemistry." Translated by R. A. Lehfeldt, 1898. Vol. 1, p. 192.

[2] Cf. W. C. McC. Lewis, "A System of Physical Chemistry," Vol. 1, "Kinetic Theory," 1918, pp. 409-10.

Arrhenius[1] considered that the difference in the condition of the molecules could be accounted for by assuming two types of molecules in any given substance. He called these "active" and "passive" molecules and assumed that an equilibrium existed between them, the concentration of active molecules being small as compared with the concentration of passive molecules. Increase in temperature would increase the concentration of active molecules and in this way account for the great increase in reaction velocity.

This view of active and passive molecules, suggested by Arrhenius in 1889 must necessarily be true since it is fundamentally a statement of the fact that all of the molecules of a substance do not react simultaneously in a monomolecular reaction, and that the number of collisions in a bi-, ter-, etc., molecular reactions are not the only factors in reactions occurring with these. It will be seen that the newer theories attempt explanations of the facts which were clearly pointed out by Arrhenius over thirty years ago.

Another angle from which to consider these relations was indicated by van't Hoff:[2] "The fact that a reaction needs time for its completion involves that, besides the cause producing it, which we may describe as the 'moving force' or 'affinity,' a 'resistance' comes into play. The two are therefore to be considered separately, and it may be foreseen that the nature of the resistance can be most varied, whilst the 'moving force' is definite for a given state of matter." This has been expressed at various times in the following form in analogy with Ohm's law of electric conduction:

$$\text{Velocity of Reaction} = \frac{\text{Driving Force}}{\text{Resistance}} \qquad (1)$$

The driving force is given by the change in free energy of the reaction. The meaning of the resistance term is not in itself very clear. Reasoning in a circle, with the driving force (or chemical affinity) constant, the change in velocity is a measure of the resistance, and any factors which change the chemical resistance change the velocity. The effect of small changes in

[1] S. A. Arrhenius, *Z. physik. Chem.* **4**, 226 (1889).
[2] J. H. van't Hoff, l.c. p. 176.

temperature may be said to be sought mainly in the change in resistance, but none of the simple effects on ordinary or common types of resistance can be used to explain or account in any satisfactory manner at present for this effect on the velocities of chemical reactions.

The relations which have been presented so far do not lead directly to a chemical interpretation of the facts but at the same time may aid in fixing the nature of the problem to be studied.

The study of the atom and molecule as such has not thrown light on this problem. However, the study in recent years of the structure of the atom and molecule in terms of negative electrons and positive nuclei and their possible arrangements and motions has made it probable that the relations developed in this way will ultimately clear up a number of these questions. A comparison of rates of ordinary chemical reactions with rates of decomposition of radioactive substances is of interest. The former are affected profoundly by rise in temperature, the latter not at all as far as experimental observations have gone. The latter, however, decompose (or react) according to the monomolecular reaction velocity law. According to the modern nuclear atom theory the difference in temperature effect is connected with the fact that in ordinary chemical reactions, the negative electrons outside the nucleus are involved, while in radioactive changes, the changes which take place occur in the positive nucleus, which is itself made up of various positive charges (hydrogen and helium positively charged nuclei) and negative electrons. In considering chemical changes here, attention will be devoted solely to the transformations which involve the numbers, positions and motions of the negative electrons outside the positive nuclei of the atoms and molecules. The radioactive changes which involve numerical changes in the charges of the positive nuclei of the atoms concerned do not come within the scope of the present treatment, although the changes are known in a number of cases with some degree of certainty.

The tendency in recent years to ascribe the chemical and physical properties of atoms and molecules to electrons, their arrangements, and motions, is involved in these considerations.

At the same time, it must be stated that there is no completely satisfactory theory at hand at present. Matters are in a state of flux and development. The views which will be presented here are therefore necessarily fragmentary, since it is not planned to give an exhaustive review of the subject, but only to indicate some of the possibilities and main lines of development. It is hoped that enough will be presented to awaken interest in these problems in chemists whose work may lie in different fields and who are therefore more or less out of touch with such views.

The negative electrons which surround the positive nucleus of an atom (the nucleus may itself contain negative electrons and it is therefore necessary to indicate which are meant) are taken to be the active agents in chemical reactions. J. J. Thomson [1] was the first to point out the importance of electron views in the molecular structures of compounds and to develop certain relations with regard to the spatial arrangements of the electrons in atoms, which showed interesting analogies with a number of chemical and physical properties of series of elements. The views of J. J. Thomson with regard to the identity of the transfer of negative electrons between atoms with valence linkings were applied by a number of workers to the structures of chemical compounds. These views are based fundamentally upon the original observations of Faraday of the laws of electric conduction in solutions and the conception of Helmholtz [2] in his Faraday lecture of 1881 with regard to the atom of electricity, but made definite and applicable to ordinary chemical structures by the experimental and theoretical studies of J. J. Thomson. The electron valence views are not necessarily connected with any particular theory of the possible electron configurations within the atom or molecule. These theories and applications of the electron conception of valence as developed by J. M. Nelson and the writer, beginning in 1909, purposely ignored such configurations. There was a great temptation to suggest hypothetical arrangements of electrons which could readily have been brought in agreement with certain properties of atoms and molecules. In view of the more or less speculative nature, at the time, of the views as developed, this was not done.

[1] J. J. Thomson, "The Corpuscular Theory of Matter," 1904.
[2] H. von Helmholtz. *Vorträge und Rede, 4te Aufl.* 2, 251; *Ges. Abh.* 3, 97.

In the last twelve years the electron conception of valence has been widely accepted. This does not mean that the theory is in any way final. Much remains to be done still and many relations to be unravelled, but it appears to be quite certain that the electron conception of valence marked a definite advance.

As the usefulness of the electron conception of valence became more apparent, and the nature of the developments became less hypothetical, the next step was taken by attempting to develop the electronic arrangements within the atoms and molecules in order to explain and account for chemical and also physical phenomena. If the chemical and physical properties of elements and compounds can be shown to be dependent upon certain definite arrangements of electrons in atoms and molecules, a great advance will have been made. Furthermore, such arrangements would then be connected with chemical changes and reactions and it would be possible to develop theories of chemical reactions upon the basis of electron arrangements and their changes within the molecules. The general point of view can be stated concisely. The molecule is taken as the unit, and the arrangement of the electrons in the molecule as a whole considered, at least in gases where the term molecule has a definite meaning. No distinction is made as to the electrons which were part of one atom or another before the combination (and accompanying electronic rearrangement) to form the molecule took place. The stable arrangement of the electrons in the molecule is the essential feature of the more recent developments. They differ from the electron conception of valence in that the latter considered the change which occurs in an atom of an element before and after combination, emphasizing this change by indicating the addition or subtraction of one or more electrons (negative or positive valence). Conclusions were then drawn with regard to the properties of the resulting combinations from the valence (or number of electrons gained or lost) and the atoms in combination, as compared with the uncombined elements.

Both methods of treatment are useful and should aid in the development of theoretical views. They are not directly dependent upon each other, although the molecular electron structures may be considered to have developed as a result of the

valence electron structures. The former considers the molecule as the unit, certain general arrangements of electrons being capable of conferring stability; the latter considers the atoms plus or minus valence electrons as the units.

It will not be necessary to enter farther into the valence electron structures in the present connection. Reference to two recent books should suffice for those interested in this part of the subject.[1]

G. N. Lewis [2] developed the idea of the so-called "cubical" atom in which the electrons in atoms arrange themselves in series of concentric shells, these electrons being stationary within limits. The innermost shell contains two electrons, all other shells tend to hold eight, each at a corner of a cube or in pairs at the corners of a regular tetrahedron. The outermost shell may hold, 2, 4, 6, or 8 electrons. When two atoms combine to form a molecule, the tendency in the molecule is to form the cube of electrons. Two or more electrons may be common to two cubical arrangements. This view was applied to a number of physical and chemical problems and interesting conclusions obtained especially with regard to certain periodic relations which occur in various series of elements.

I. Langmuir extended these views in a number of directions. It will be impossible in the space available here to give even a short outline of the applications which he has made to chemical and physical phenomena. The most satisfactory procedure seems to be to give the postulates which he found were necessary in order to develop the theory of the molecular electron structures. These will serve to show the underlying concepts and indicate the scope of the views. These postulates were given by him, as follows: [3]

"1. The electrons in atoms are either stationary or rotate, revolve, or oscillate about definite positions in the atom. In the most stable atoms, namely those of the inert gases, the electrons have positions symmetrical with respect to a plane, called the equatorial plane, passing through the nucleus at the center of the atom. No electrons lie in the equatorial plane. There is an axis of symmetry (polar axis) perpendicular to this

[1] H. S. Fry, "The Electronic Conception of Valence and the Constitution of Benzene"; Longmans, Green & Co., 1921; K. G. Falk, "Chemical Reactions; Their Theory and Mechanism," 1920.

[2] *Jour. Amer. Chem. Soc. 38*, 762 (1916). The theory of W. Kossel (*Ann. Physik. 49*, 229 (1916)) is similar to that of Lewis in a number of respects and will therefore only be referred to in this connection.

[3] I. Langmuir, *Jour. Amer. Chem. Soc. 41*, 868 (1919).

plane through which four secondary planes of symmetry pass forming angles of 45° with each other. These atoms thus have the symmetry of a tetragonal crystal.

"2. The electrons in any given atom are distributed through a series of concentric (nearly) spherical shells, all of equal thickness. Thus the mean radii of the shells form an arithmetic series 1, 2, 3, 4, and the effective areas are in the ratios 1; 2^2; 3^2; 4^2.

"3. Each shell is divided into cellular spaces or cells occupying equal areas in their respective shells and distributed over the surface of the shells according to the symmetry required by Postulate 1. The first shell thus contains 2 cells, the second 8, the third 18, and the fourth 32.

"4. Each of the cells in the first shell can contain only one electron, but each other cell can contain either one or two. All the inner shells must have their full quotas of electrons before the outside shell can contain any. No cell in the outside layer can contain two electrons until all the other cells in this layer contain at least one.

"5. Two electrons in the same cell do not repel nor attract one another with strong forces. This probably means that there is a magnetic attraction (Parson's magneton theory) which nearly counteracts the electrostatic repulsion.

"6. When the number of electrons in the outside layer is small the arrangement of the electrons is determined by the (magnetic?) attraction of the underlying electrons. But when the number of electrons increases, especially when the layer is nearly complete, the electrostatic repulsion of the underlying electrons and of those in the outside shell becomes predominant.

"7. The properties of the atoms are determined primarily by the number and arrangement of electrons in the outside shell and by the ease with which the atom is able to revert to more stable forms by giving up or taking up electrons.

"8. The stable and symmetrical arrangements of electrons corresponding to the inert gases are characterized by strong internal and weak external fields of force. The smaller the atomic number, the weaker the external field.

"9. The most stable arrangement of electrons is that of the pair in the helium atom. A stable pair may also be held by (a) a single hydrogen nucleus; (b) two hydrogen nuclei; (c) a hydrogen nucleus and the kernel of another atom; (d) two atomic kernels (very rare).

"10. The next most stable arrangement of electrons is the *octet,* that is, a group of eight electrons like that in the second shell of the neon atom. Any atom with atomic number less than 20, and which has more than 3 electrons in its outside layer, tends to take up enough electrons to complete its octet.

"11. Two octets may hold one, two, or sometimes three pairs of electrons in common. One octet may share one, two, three, or four pairs of its electrons with one, two, three, or four other octets. One or more pairs of electrons in an octet may be shared by the corresponding number of hydrogen nuclei. No electron can be shared by more than two octets."

These postulates, developed as the result of the study of the physical and chemical properties of a number of substances, will serve as a system of classification of the properties of such substances. It is interesting to note that on the Lewis-Langmuir view, a single valence linking is represented by two electrons

held in common by the two atoms, a double valence by four electrons, etc.[1]

Langmuir also indicated the contradiction in the structure of the atom on the octet or cubical view with the structure of the Bohr atom in which the electrons are assumed to revolve in one plane in orbits about the nucleus. Since the Bohr atom has been successful in connection with the study of the spectra of hydrogen, helium, and lithium, possible explanations of the contradiction were suggested.

A still more recent theoretical development along the line of atomic and molecular electron structure is that of J. J. Thomson.[2] The electrons in an atom are assumed by him to be in equilibrium because of their mutual repulsions and the attraction of the positive nucleus. The laws governing these repulsions and attractions are developed. The conditions of stability in the arrangement of electrons around a central positive charge are given. It is shown that for eight electrons the cube is not the stable arrangement but rather a twisted polyhedron with eight triangular faces and two four-sided ones. One to eight electrons may exist on the surface of a sphere surrounding a corresponding positive charge. With a positive charge equal to nine, eight electrons will form a spherical shell concentric with the central charge, and one electron will go outside to find a position of stable equilibrium, etc. The periodicity, as in most such arrangements of electrons, is similar to that expressed in the periodic system. Other regularities are brought out. Molecules are formed by electrons of the atoms acting as couplings; each valence bond involving two electrons, one from each atom. The molecules which survive (a number which may have transitory existence are indicated) are those which show the smallest tendency to attract other molecules, "the law of survival of the unattractive." A number of structures, both simple and more

[1] For various developments and applications of these views cf. among others I. Langmuir, *Jour. Amer. Chem. Soc. 42*, 274 (1920); W. M. Latimer and W. H. Rodebush, *Jour. Amer. Chem. Soc. 42*, 1419 (1920); R. N. Pease, *Jour. Amer. Chem. Soc. 43*, 991 (1921); C. R. Bury, *Jour. Amer. Chem. Soc. 43*, 1602 (1921); E. J. Cuy, *Z. Elektrochem. 27*, 371 (1921); J. R. Partington, *Nature 107*, 172 (1921); A. O. Rankine, *Nature 107*, 203 (1921); A. W. C. Menzies, *Nature 107*, 331 (1921); H. S. King, *Jour. Amer. Chem. Soc. 44*, 323 (1922); E. D. Eastman, *Jour. Amer. Chem. Soc. 44*, 438 (1922).

[2] "The Structure of the Molecule and Chemical Combination," *Phil. Mag. (VI), 41*, 510-544 (1921).

complex are indicated, and other properties discussed, but it would lead too far to enter into these here.

Very recently, G. N. Lewis [1] has suggested that a tetrahedral arrangement of the electrons in the outer sphere of an atom with two electrons at each apex, when an atom is in combination, would be a more satisfactory representation, each pair of electrons standing for a chemical linking.

The striking features of these various developments to which it is desired to draw attention in the present connection are, first, the more or less definite structures or arrangements of the electrons in the molecules which are assumed to confer stability on the chemical union or compound, and secondly, taking into account the relative sizes of electrons, nuclei, atoms, and molecules, that only a very small part of an atom is actually directly active in a chemical linking. Chemical architecture has gone beyond the atom in the molecule and is using the electron in the atom and in the molecule. Whatever directions developments in these lines may take, electronic structures of atoms and molecules will surely play an increasingly important part in the classification of chemical compounds and reactions and in helping to answer questions involving stability and reaction velocity.

These views of electronic structures of molecules as well as of atoms represent the most recent developments in chemical structures. A possible weakness lies in the fact that such structures apparently assume fixed positions for the outer electrons. This difficulty was of course clearly recognized by Lewis and by Langmuir, and certain assumptions were made with regard to their motions, possibly vibratory, within certain limits to overcome this, and at the same time to account for certain physical properties such as the relative positions of spectral lines, etc.

It is interesting to note that the number eight which occurs so frequently in these electronic structures, first in the J. J. Thomson model, then in the cubical and tetrahedral models, is the modern way of indicating the same relation which led D. Mendeléeff as a result of the grouping of the elements in his Periodic System to state that for many elements which combine with oxygen and with hydrogen, the sum of the maximum va-

[1] G. N. Lewis; Nichols lecture, delivered before the New York Section of the American Chemical Society, May, 1921.

lences which any one element shows in these two compounds is eight. The same fact has been brought out repeatedly in different ways such as stating that the extreme difference in valence which an atom can show is eight electrons, etc. The spatial arrangements are in the first instance a mechanical model of such statements.

Matter is considered to be made up of positive units and negative units. The negative unit is the negative electron of a certain mass and size with a unit negative charge. The positive unit has been termed the "proton" and consists of a hydrogen atom with a unit positive charge, a mass 1800 times as large as that of the negative electron and a volume 1800 times smaller. Striking confirmation of the general theory of the composition of matter was given recently by Rutherford.[1] Rutherford found experimentally that from the positive nuclei of the elements nitrogen, boron, fluorine, sodium, aluminium, and phosphorus, by the passage of swiftly moving α particles (from radium C for example), positively charged hydrogen atoms (protons) were separated. These charged hydrogen atoms moved with great speeds, showing penetrating powers of from 40 centimeters to 90 centimeters in air. Such hydrogen atoms carrying unit positive charges could only have come from the disintegration of the positive nuclei of the indicated elements. Of the elements examined in this way, only the six mentioned above could be broken up. The atomic masses of these elements are given by the expressions $4n + 2$ or $4n + 3$, in which n is a whole number. Elements of mass 4n (such as carbon, oxygen, and sulfur) showed no effect. The explanation was advanced that the nuclei of the six elements decomposed are built up of helium nuclei (mass 4) and of hydrogen nuclei.

The present view of the atom, then, pictures a complex system consisting of a central region in which is concentrated a certain number of positive charges and negative electrons, the number of positive charges being in excess of the negative, and an outer region containing a number of negative electrons corresponding to the excess positive charge of the central region, arranged in certain configurations and with more or less restricted motions.

[1] E. Rutherford, *Phil. Mag.* *37*, 538 (1919); Bakerian Lecture, *Proc. Roy. Soc. London* (*A*) *97*, 374 (1920); E. Rutherford and J. Chadwick, *Phil. Mag.* *42*, 809 (1921).

The actual volume of the atom is that included within the sphere of action, if it may be called so, of the system of positive nucleus plus surrounding electrons. Because of the small volumes of the nucleus and electrons, the actual volume of the atom so occupied will be very minute with comparatively immense empty spaces composing the major part of the atom. The forces, whether gravitational, electrical, or of other nature, which act to maintain the compositions and configurations, do not enter directly at present into the problem under discussion. The point to which it is desired to call attention is that in such a structure, which may be of varying and considerable complexity with different atoms, it is readily conceivable that a certain part of the atom might react and not the rest. This is comparable to those reactions of organic and also other compounds, in which, by a suitable choice of reagents and conditions it is possible to bring about a reaction with an atom or grouping of that compound and leave the rest of the molecule apparently unaffected. Views similar to this have been considered by Trautz [1] and by Stern [2] as necessary in the reactions between two or more molecules, where, not only must there be a meeting of the two in order to have reaction possible, but the meeting must take place between two definite parts of the molecule. This factor, called the "steric" factor is not considered to be the same as saying that the molecules must be in an active state, but is an additional factor. Further, it may also be pointed out that atoms in complex molecules are not assumed to be fixed in position, but have a certain motion of their own. The only requirement in the chemical molecule is that the atoms are not free to take up any motion whatsoever, but are controlled by certain other atoms with which they are said to be directly combined. This combination involves a rearrangement of negative electrons outside the nucleus, either in the general terms in which the exact positions are not specified as in the electron valence theory, or in the more specific configurations postulated in the different molecular electron theories. The motions of these atoms as such might be considerable. The same is true for the arrangements and motions of the electrons in an atom.

[1] M. Trautz, *Z. anorg. Chem.* *106*, 149 (1919).
[2] O. Stern, *Ann. Phys.* *44*, 497 (1914).

The electrons in a molecule are considered to be arranged in definite more or less stable configurations which determine the chemical and physical properties of the substances. Here again, reaction may occur because of certain electrons, or electron arrangements, or electron motions. This leads to a possible suggestion with regard to the rate of reaction of a single substance undergoing change. This substance possesses certain electron arrangements and these electrons have motions of their own, possibly vibratory, within limits. As long as a certain configuration persists, the substance is stable, but if in the internal motions of the electrons more stable configurations are reached in certain instances, in which possibly a breaking up of certain atomic linkings or rearrangement of valence electrons occurs, then so-called chemical reaction is said to take place. In such an explanation of chemical action, the question of velocity of motion of the electrons does not appear to be involved necessarily, although it is probable that it may play a part. It is essentially a question of configurations of varying degrees of stability. More complex molecules should show more possibilities of reaching different configurations of greater stability than less complex molecules and might therefore show greater possibilities of reaction. In the absence of external influences, with a given species of molecules, it is a question of chance, or better perhaps, of probability, as to the number of molecules which would be in the favored configuration for reaction at any instant. This hypothetical view may be the explanation for the monomolecular reaction velocity law. The views involving radiation phenomena which will be presented presently, appear to be based upon such considerations if a mechanical model of the atom or molecule is thought of, but in the actual developments such models are ignored, and the theoretical concepts are independent of these configurations, at the present time, at any rate.

Any factor, therefore, which may influence the electron configurations and limited motions, may influence the rate of change into more stable configurations. The predominating influence is here placed on the outside negative electrons. The positive nuclei are not considered as taking a prominent part in the chemical reactions. They are assumed simply to be associated with the negative electrons. At the same time it must be stated

that while attention is just now fixed on the negative electrons, their configurations and motions, as the dominating feature in chemical reactions, it must be remembered that these configurations and motions are controlled by the positive nuclei. Some time in the future the point of view may be shifted and the properties of the nuclei used as the underlying causes for the various phenomena.

In studying the arrangements and motions of electrons in atoms and molecules, the properties which appear to be of most value are those involving the various forms of radiation. Radiation phenomena appear to offer the most hope for a successful study of the properties of the electrons within atoms and molecules, including under these properties such factors as the motions and arrangements of the electrons and the changes in these motions and arrangements under the influence of outside agencies. Considerable work is being carried on at the present time on radiation problems in connection with chemical changes. Some of the theoretical developments which have resulted from such studies will be presented. It will be impossible to give a definite statement of the present status of the subject with regard to final or even satisfactory theories. Work is in progress in a number of places, and the views presented may, in part, be contradictory, but they will serve to show the trend the work is taking, and also possibly indicate solutions to certain definite problems.

Arrhenius [1] showed in 1889 that the effect of temperature on the reaction velocity could be represented by the equation

$$\frac{d \log_e k}{dT} = \frac{A}{T^2} \tag{2}$$

or, in the integrated form,

$$\log_e \frac{k_2}{k_1} = A\left(\frac{1}{T_1} - \frac{1}{T_2}\right) \tag{3}$$

in which k denotes the reaction velocity constant at the absolute temperature T, or k_1 and k_2 the velocity constants at tempera-

[1] S. A. Arrhenius, *Z. physik. Chem.* *4*, 226 (1889). Cf. also E. C. C. Baly and F. O. Rice, *J. Chem. Soc.* *101*, 1475 (1912).

tures T_1 and T_2, and A, a constant which is very nearly independent of the temperature for a given reaction.

Equations (2) and (3) are similar in form to the van't Hoff equation connecting the heat evolved in a chemical reaction with the equilibrium constant and the temperature. Arrhenius deduced his equation on the basis of the presence of passive and active molecules and of the existence of an equilibrium between the two forms, the term A representing one-half the energy required to transform one mol of the passive form of the reacting molecules into the active form (or AR representing the energy to transform one mol in this way). The Arrhenius equation holds fairly satisfactorily for a number of reactions which have been studied, but the theoretical assumptions which appear to be involved in the deductions are somewhat uncertain. The equation, while representing the experimental facts, must therefore be looked upon as empirical in so far as the deductions of Arrhenius are concerned.

Much of the more recent work on these questions has involved expressions of the form of the Arrhenius equation, which appears to represent the facts in a satisfactory manner, together with attempts to base these upon more satisfactory bases or assumptions. From the point of view of statistical mechanics, Marcelin [1] and Rice [2] showed that the relation between reaction velocity and temperature may be given by the equation

$$\frac{d \log_e k}{dT} = \frac{E}{RT^2} \qquad (4)$$

In their deductions it was assumed that the condition for a molecule reacting is brought about by the attainment of a certain critical value for its internal energy. The term E in the equation denotes the difference between this critical value and the average internal energy per gram molecule, and was therefore later called by W. C. McC. Lewis the "critical increment." As developed by Rice, E in equation (4) is given by the expression $V_c - V_m + 1/2\,RT$, in which V_c equals the critical value of the internal energy of the molecules, and V_m the mean value of the potential energy of the molecules. These deductions did not sug-

[1] R. Marcelin, *Ann. phys.* 3, 120 (1915).
[2] F. O. Rice, *Rep. Brit. Ass'n.* 1915, 317.

gest any mechanism by which this increase in energy from the mean to the critical value is brought about. Such a possible mechanism was given in a series of papers by W. C. McC. Lewis and tested experimentally in a number of ways. "The hypothesis is that the increase in internal energy which a molecule must receive before it is capable of reacting (that is, the critical increment E) is communicated to it by infra-red radiant energy present in the system, the addition of energy being made in terms of quanta of the absorbable type. . . . The principal feature of the hypothesis is the introduction of the quantum theory into the problem of chemical kinetics, the effect of temperature, and catalysis."[1] Lewis adopted the view of the action of infra-red radiation "which was necessarily present throughout any system in virtue of its temperature" as possibly "the active agent in promoting chemical changes of the ordinary or thermal type, such changes including not only the so-called uncatalysed reactions, but catalysed reactions as well, in so far at least as these are met with in homogeneous systems, and further that the influence of temperature on velocity might be explained on the same basis." Lewis also showed that

$$E = N\ h\ \gamma \qquad (5)$$

in which N equals the number of molecules in one gram molecule of substance (6.062×10^{23}), h, Planck's constant (6.5×10^{-27} erg-seconds), and γ a single frequency of vibration which was taken to be the effective frequency in the change which was occurring. This expression is a statement of the Einstein law of the photochemical equivalence applied to infra-red radiation.

According to the view of Lewis, in catalytic actions, the catalyst absorbs the infra-red radiation and transmits this energy to the reacting molecules which are themselves not capable of absorbing these radiations. This brings catalytic actions in line with chemical reactions in general, except that with reactions not included under catalysis the reacting molecules themselves absorb the infra-red radiation directly.

The experimental verification of Lewis' original views was not entirely satisfactory. For a bimolecular homogeneous reaction, such as the decomposition of gaseous hydrogen iodide,

[1] W. C. McC. Lewis, *J. Chem. Soc. 109*, 798 (1916).

fairly good agreement was obtained between the energy increment E as calculated by means of the reaction velocity constants for two different temperatures, and as calculated from the infrared vibration frequency on the basis of the Einstein law. On the other hand, the agreement for the monomolecular reactions was not nearly as satisfactory, and in fact, in some cases such as the rate of dissociation of phosphine, the disagreement was too great (of the order of 10^7) for the relation to be considered valid. It must be mentioned, however, that in these deductions the index of refraction of the mixture was assumed to be unity. This factor was brought out in more recent publications by Lewis as will be mentioned presently.

Equation (4) written in different forms has formed the basis for investigations by a number of workers in the last years. The formulation employed most frequently involved the term Q in place of E and the expression of the equation in the exponential form is as follows:

$$k = s\, e^{-Q/RT} \tag{6}$$

in which k, as before, denotes the specific reaction rate, s a quantity with the dimensions of time, and Q, a quantity with the dimensions of energy and found experimentally to be very nearly constant within certain more or less extended ranges of temperature, and known variously as "heat of activation," "energy of activation," and "critical increment."

The quantity Q has been interpreted in various ways. For example, Arrhenius, as already pointed out, considered it to be the heat of reaction accompanying the transformation of the "passive" form of molecules into the "active" form; Marcelin and Rice, the energy of their "active" state minus their mean energy; Trautz,[1] one of the first workers to consider the infrared radiation as playing an important part in chemical actions, calculated this "heat of activation" from the "heats of activation" of individual atoms by empirical rules; W. C. McC. Lewis and Perrin [2] placed $Q = Nh\gamma =$ the radiant energy of activating frequency γ which must be absorbed to put the molecules into

[1] Cf. *Z. anorg. Chem. 102*, 81 (1918), for a summary of the work of Trautz, also *Ibid., 106*, 149 (1919).
[2] J. Perrin, *Ann. phys.* [9] *11*, 5 (1919).

the reactive condition; Tolman[1] on a statistical mechanical basis puts Q equal to the mean energy of molecules and modes of electromagnetic vibration when these take part in a reaction minus their mean energy whether or not they are in a reactive condition; and S. Dushman[2] placed $Q=Nh\gamma$ similarly but specified no mechanism of activation.

With regard to the significance of the term s which has the dimensions of frequency, for a monomolecular reaction Trautz developed an equation in which its value depended on the number of collisions between the constituent parts within the molecule. Lewis developed several different ways of evaluating s. The recent suggestion of Dushman, placing s equal to γ suggested interesting possibilities. Tolman[3] pointed out in this connection the probable limitations of Dushman's method of procedure, and that Q is in general not constant nor does it correspond to a single vibration frequency. He showed that using the assumptions given in discussing the value of Q,

$$k = e \int \frac{Q}{RT^2}\, dT, \tag{7}$$

and assuming Q to be constant, that

$$k = s\, e^{-Q/RT} \tag{6}$$

in which s is also constant. In general, however,

$$k = e \int \frac{dQ}{RT} e^{-Q/RT} = s\, e^{-Q/RT} \tag{8}$$

in which $s = e^{\int \frac{dQ}{RT}}$ is a variable and therefore could not be put equal to a single frequency, as Dushman assumed. For bimolecular reactions, s has been put proportional to the number of collisions between the molecules of the substances reacting at the temperature in question. This proportionality, however, includes the factor of the state of the molecules spoken of in connection with monomolecular reactions.

[1] R. C. Tolman, *Jour. Amer. Chem. Soc.* *42*, 2506 (1920).
[2] S. Dushman, *Jour. Amer. Chem. Soc.* *43*, 397 (1921).
[3] R. C. Tolman, *Jour. Amer. Chem. Soc.* *43*, 269 (1921).

The experimental material which is available to test the equations which have been given is rather scant. The general equation which is used has the following form

$$k = s\, e^{-Nh\gamma/RT} \qquad (9)$$

as already indicated, in which, from quantum theory considerations, $Q = Nh\gamma$ = energy of activation of one gram molecule of substance. To test this equation, values of k determined experimentally at different temperatures may be used, and the value of Q determined. From this, the radiation frequency γ which should be the activating radiation may be calculated. On the other hand, from the absorption spectrum of the substance, it should be possible to calculate the velocity constant of the reaction.

A few reactions occurring in the gaseous phase have been studied in this way, but the data are not complete enough for a general discussion.[1] In fact, it seems to be still necessary to make certain assumptions in applying the theoretical equations to the experimental results. Thus Tolman [2] showed, in reviewing the previous work, that the views of Perrin (and also of others) involved the assumption that in activating a substance, light of a single frequency or of a very narrow range of frequencies only would be involved. Experimentally it has been found that photochemical reactions are brought about by light over a considerable range above the limiting threshold frequency. Langmuir [3] showed that the two tests of the radiation hypothesis, (1) that the reacting substance must absorb radiation of the frequency required to produce activation and that therefore there must be an absorption band which includes this frequency, and (2), that the total amount of radiant energy absorbed must be sufficient to supply the known heat (or energy) of activation to the molecules which reacted, do not hold with the reactions for which data were available (decomposition of phosphine, dissociation of hydrogen, iodine, and of nitrogen peroxide). He considered that the form of the Arrhenius equa-

[1] Cf. W. C. McC. Lewis, Trautz, Tolman, etc., also F. Daniels and E. M. Johnston, *Jour. Amer. Chem. Soc.* *43*, 53, 72 (1921), for results on the decomposition of nitrogen pentoxide.
[2] R. C. Tolman, *Jour. Amer. Chem. Soc.* *42*, 2506 (1920).
[3] I. Langmuir, *Jour. Amer. Chem. Soc.* *42*, 2190 (1920).

tion (equation (1)) was due to its being based upon statistical laws, assuming "that the chance that a given molecule will undergo a chemical reaction is proportional to the probability that it contains a specific amount of energy." "The similarity between the Arrhenius and the Wien (radiation) equation thus results from the fact that reaction velocity and radiation are fundamentally dependent upon phenomena involving probability. Both equations can be derived from the same statistical law . . . the energy for activation of molecules must be derived from internal energy of the molecules." Langmuir also spoke of a sort of "trigger" action which is necessary to bring about chemical action in a molecule. Tolman, on the other hand, attempted to overcome the difficulties by a more general derivation of the kinetic equations on the basis of statistical mechanics, but did not apply his deductions to definite cases.

Baly [1] has taken hold of the problem from a different angle. His fundamental premise is that "the observed deviations from Einstein's law of photochemical equivalence might very possibly be due to the re-absorption by the surrounding reactant molecules of the energy radiated during the reaction." "According to this law, when a reaction takes place photochemically, the absorption by a molecule of an amount of energy equal to one quantum at its absorbing frequency results in that molecule undergoing reaction, and the number of quanta absorbed and the number of molecules reacting must be equal. A study of many photochemical reactions has, however, shown that except in one case the number of molecules reacting is far in excess of the number of quanta absorbed." "In any photochemical reaction it is obvious that the first stage is the absorption of the light energy, and that the whole can be written

$$A + E = B + E + K$$

where A and B are the reactant and resultant molecules respectively, E is the amount of light energy absorbed, and K is the ordinary observed heat of the reaction. Now the molecule A

[1] E. C. C. Baly, *Phil. Mag.* (*VI*) *40*, 15 (1920); E. C. C. Baly and W. F. Barker, *J. Chem. Soc. 119*, 653 (1921); cf. also F. Daniels and E. M. Johnston, *Jour. Amer. Chem. Soc. 43*, 53, 72 (1921) on the thermal and photo-chemical decomposition of nitrogen pentoxide, and E. C. C. Baly, I. M. Heilbron and W. F. Barker, *J. Chem. Soc. 119*, 1025 (1921), on "The Synthesis of Formaldehyde and Carbohydrates from Carbon Dioxide and Water."

absorbs the energy E at its characteristic frequency, and the minimum value of E is one quantum at that frequency. On the other hand, it is evident that the whole of the energy on the right hand side must be radiated at frequencies characteristic of the resultant molecule B, that is to say, the total energy radiated during the reaction must be equal to an integral number of quanta at frequencies characteristic of B. It has previously been shown that the frequencies of any molecule are integral multiples of the frequencies of its atoms, and since the molecules A and B have at any rate some atoms in common, it follows that they must have frequencies in common. It was therefore suggested that whereas Einstein's law must hold if the energy radiated during a reaction is dissipated to the surroundings, the fact that A and B have frequencies in common will result in some of this energy being absorbed by further molecules of A. If the amount thus reabsorbed is sufficiently great, more than one molecule of A will react for every quantum absorbed." This view was tested by means of the photochemical reaction between hydrogen and chlorine, for which Einstein's law had been found not to hold. It was found that with a given light intensity the amount of hydrogen chloride formed in unit time was at first small and then rapidly increased up to a constant maximum. The constant maximum rate of formation of hydrogen chloride was not proportional to the intensity of the light. The divergence from Einstein's law of photochemical equivalence depended on the intensity of the light and rapidly increased with the intensity.

Baly concluded that the evidence for the reabsorption of radiated energy in a chemical reaction was satisfactory and accounted for the fact that the laws developed from the quantum theory and the radiation hypothesis did not hold. This view leads to new and striking developments with regard to these relations, and while apparently not simplifying them, promises to furnish more satisfactory bases for the theoretical and experimental developments.

A somewhat different explanation of these relations was suggested by Lewis and McKeown.[1] In several monomolecular

[1] W. C. McC. Lewis and A. McKeown, *Jour. Amer. Chem. Soc. 43*, 1288 (1921).

reactions, the observed velocity constants were 10^7 times as great as those calculated on the basis of continuous absorption by the oscillator (electron), with the refractive index taken to be unity. These discrepancies are referred to the assumed value for the refractive index, which it is stated in this last article actually should refer to the individual molecules, and be of considerably greater magnitude. The following expression was developed:

$$k_{mono} = \frac{8\pi^2 \, e^2 \, n_m^3 \, \nu^2}{3mc^3} \cdot e^{-h\nu/kT} \qquad (10)$$

in which k_{mono} represented the monomolecular reaction velocity constant, e and m the charge and mass of the electron, ν the frequency of the radiation characteristic of the reaction, h and k the constants of Planck and of Boltzmann, T the absolute temperature, and n_m the refractive index of the substance in an ideal state corresponding to the closest possible packing of the molecules. This term n_m was shown in several ways to have a value approximately 200, practically independent of the system considered and of the temperature. This expression was shown to agree satisfactorily with the experimental data for monomolecular reactions, so far as these were available. Criticisms of the radiation theory were also considered in this article, and especial emphasis placed on the distinction between thermal and photochemical processes, which were confused in some of these criticisms. In photochemical reactions, the temperature of radiation is greater than that of the material on which it acts, while in thermal reactions, the temperatures of the radiation and of the material are identical.

In discussing certain criticisms of Marcelin's views, Adams [1] presented some relations which are of interest because of their fundamental character, and may therefore be quoted: "In the last few years many attempts have been made to apply the quantum theory to problems of chemical dynamics. Some of these applications have made use of a quantum theory in a rather more definite form than has been found necessary in the physical applications where the theory has had much success.

[1] E. P. Adams, *Jour. Amer. Chem. Soc.* *43*, 1251 (1921).

If the laws of chemical dynamics are found to be consistent with the principles of statistical mechanics it would seem to be not only unnecessary, but unjustifiable, to introduce the quantum theory in order to derive these laws. That the quantum theory is of importance in general chemical theory is probable; neither statistical mechanics nor the first two laws of thermodynamics give any information as to the constants which enter into the various thermodynamic functions. These constants depend upon the behavior of systems at or near the absolute zero of temperature, and it is in this region that the quantum theory has had considerable success. But this is quite a different matter from assuming that the mechanism of chemical reactions and transformations requires the use of the discontinuities inherent in any form of a quantum theory."

The recent theories of chemical reactions have been presented here in a somewhat disjointed form. There is not at present an agreement among the different workers as to the most probable and most useful view to be adopted with regard to the application of the radiation phenomena, quantum theory, etc. It was therefore considered preferable to present the views of some of the individuals who are actively engaged upon these problems, even if these views contradict each other in some respects, rather than to attempt a summary or outline of the present status of the problem, since the problem is continually presenting new aspects and developing novel features. It is evident that the theoretical deductions with reference to the phenomena underlying the kinetics of monomolecular (and, of course, also of polymolecular) reactions are not as yet in definite form. The radiation and quantum theories have given some new and interesting points of view, which in all probability will ultimately lead to a more satisfactory theory with respect to many of the relations.

In brief, the views which appear to have been generally accepted are as follows: The cause of the monomolecular reaction velocity law is to be found in the electronic arrangements in the atoms and molecules and the changes in these arrangements due to certain vibratory motions; certain configurations are responsible for the occurrence of chemical changes (or electronic rearrangements), the frequency of the occurrence of these configura-

tions obeying some law of probability; radiant energy may play an important part in bringing about certain configurations and changes in configurations, but radiant energy in bringing about such configurations and changes is not absorbed according to the simple Einstein law of photochemical equivalence.

The suggestion made earlier in this chapter may be repeated here, namely, that a very limited portion of the electronic structure of an atom or a molecule is involved in a chemical reaction, or that in the course of the motions of the electrons, certain relative positions are arrived at, the frequency of the occurrence of such positions being given by some form of the probability law. These relative positions either bring about a further rearrangement of electrons or cause the first step of a series of such changes whose net result is ultimately called a chemical reaction. Such a view is analogous in some respects to the "trigger" action assumed by Langmuir and by others.

It might be considered that the next question to be taken up here would involve the theories of the electronic arrangements and motions in atoms and molecules. The Bohr atom may be cited as an illustration of such a theory. It would lead too far, however, to go into these questions as the results are not at all conclusive as yet. Only for the simplest elements such as hydrogen and helium, are the models which have been proposed, at all satisfactory. Further work along these lines will unquestionably lead to more satisfactory theories, but for the present, reference to some of the published work is all that is possible here.[1]

The relation of the more recent theories of chemical actions to catalytic actions has been considered only incidentally in this chapter. Any theory of chemical actions developed without limiting their nature or type must necessarily be applicable as well to catalytic actions.

[1] Cf. J. W. Nicholson, *J. Chem. Soc. 115*, 855 (1919), "Emission Spectra and Atomic Structure"; J. H. Jeans, *J. Chem. Soc. 115*, 865 (1919), "The Quantum Theory and New Theories of Atomic Structure"; I. Langmuir, *Science 53*, 290 (1921), "The Structure of the Static Atom"; *Physical Review 17*, 339 (1921), "The Structure of the Helium Atom"; R. A. Millikan, *Physical Review 18*, 456 (1921), "Some Facts Bearing on the Structure of Atoms, Particularly of the Helium Atom"; and others.

Chapter VI.

Enzyme Actions.

Enzymes are generally defined as catalysts produced by living matter. This definition replaces the single term "enzyme" by the two terms "catalyst" and "living matter." At first sight it would appear that the significance of enzymes might be obscured by the introduction of two new factors which apparently are as difficult to define as the original term. It must be pointed out, however, that the new terms make possible a comparison with phenomena which are not obviously connected with the original term and in this way aid in the consideration of enzymes from various points of view and in relation to different phenomena. The use of the definition is therefore justified. An attempt will be made in this chapter to review briefly some of the phenomena of enzyme actions especially in relation to other chemical actions.

The chemical changes in living matter are similar to the chemical changes occurring in non-living matter. That is to say, the laws governing the chemical transformations are the same for the phenomena of living and non-living matter, so far as known. Many of the substances in living matter are of great complexity. This complexity alone does not distinguish such substances from substances in non-living matter, where compounds equally complex are known. At the same time a difference is seen in the fact that many of the former, as long as they form part of the living matter, undergo change at a fairly rapid rate at moderate temperatures. The changes which may take place in a given substance need not be the same in different forms of living matter. For example, a given protein which is used as food by different animals will be transformed so that in each case the protein or other nitrogenous substances characteristic for a definite animal species will be formed. The mech-

anism of such changes involves the breakdown of the special protein to the simpler constituents such as amino acids followed by the building up of the protein or other substance necessary for the animal in question, and elimination of material not required. Analogous changes may occur with fats, carbohydrates, etc. These substances are all of varying degrees of complexity, frequently of unknown chemical structure, and in some cases even of unknown chemical composition. The changes take place at moderate temperatures and under conditions which, outside the living animal, would result in extremely slow transformations. Also the changes in the living body occur along definite lines producing definite products from substances which would permit of a great number of possible products. With plants or living vegetable matter, the relations are, in principle, the same.

Changes similar to those which occur in living matter, can in many cases be brought about by preparations obtained from such matter. The actions of such preparations are known as enzyme actions, and it is apparent that they would be included under catalytic actions with any of the ordinary definitions of the latter. No attempt is made in this preliminary survey to define life. The chemical reactions of living matter are being considered, and these are characterized by changes occurring in definite ways, peculiar in any one case to the system under investigation. It may be recalled that Berzelius enumerated such changes in one of his earliest descriptions of phenomena to be included under catalysis.[1]

Enzyme actions may perhaps be surveyed best from two points of view; first, as dependent upon the enzyme preparations producing the actions, and second, as dependent upon the chemical reactions involved. These two points of view will overlap to some extent.

The chemical study of enzyme actions as ordinarily carried on consists almost entirely of the investigation of the actions of enzyme preparations on substances *in vitro*. While enzyme studies can be carried on to a certain extent *in vivo*, the amount of this kind of work has been comparatively small, and although of the greatest interest has been more in the nature of testing hypotheses and conclusions obtained from the work *in vitro*

[1] Cf. Chapter I, p. 12.

where more accurate control of the conditions was possible. The evidence for the presence of an enzyme in a preparation is taken to be an increase in the velocity of a definite chemical reaction as a result of the addition of the preparation, or if a chemical reaction can occur so as to form two or more sets of products, a change in the relative proportions of the sets of products due to the addition of the preparation.

The chemical reactions which may be mentioned as involved in enzyme actions include the two great groups of hydrolysis reactions and oxidation-reduction reactions. Under hydrolysis reactions are included the hydrolysis of esters and fats to form alcohols and acids; of complex carbohydrates to form simpler carbohydrates, including starches, polysaccharides such as sucrose, etc., to form finally monosaccharides; of proteins and their derivatives, to form simpler bodies and finally amino-acids; of urea, to form ammonia and carbon dioxide; and of many additional classes of substances, most of which are represented by various derivatives in living matter. Under oxidation-reduction reactions are included the oxidations (and also the reductions) which occur in the chemical reactions taking place in living matter, either by the participation of the oxygen of the air, or indirectly by the oxygen of the air forming peroxides with certain organic substances present which then react farther, or by inter- or intra-molecular oxidation and reduction without involving any substances from without.

Enzyme preparations can be obtained from many sources. By choosing the material which in the living plant or animal is associated with a certain chemical transformation of definite substances, preparations can be obtained which take part in the same or analogous reactions *in vitro*. Thus, pancreas preparations will hydrolyze proteins, starches, and fats; potato preparations will hydrolyze starch; many plant and tissue preparations will show oxidizing actions; etc.

The qualitative or descriptive study of enzyme actions may proceed from two points of view. In the first place, attention may be fixed upon a certain chemical reaction and a search made for animal and vegetable materials such as tissue extracts, vegetable extracts, etc., which give evidence for the requisite actions. Secondly, a definite preparation may be tested with a number of

different chemical reactions in order to determine the different enzyme actions it possesses. Such studies have been carried on extensively. For the detailed results reference must be made to the larger compilations on enzymes. Some of the actions and behaviors of enzymes more pertinent to the general phenomena of catalysis and related to similar reactions which occur in the absence of enzymes will be discussed here. An attempt will be made to emphasize the more quantitative aspects of the problem. Before proceeding to those, some of the general properties of enzyme preparations may be mentioned.

In the first place, no enzyme is known in a state of purity as a chemical individual. Practically all enzymes exist as colloids or are intimately associated with substances having colloidal properties. The methods used for obtaining and purifying enzyme preparations are essentially the same as those used in obtaining preparations from biological materials in general, with the important reservation, which will be spoken of in more detail presently, that the treatments such as addition of acids or alkalies or heating must be eliminated to a great extent, and also a number of reagents must not be used, as otherwise the enzyme property is lost or destroyed. Water extraction, extraction by neutral salt solutions, or by glycerin solution, or by other mixtures, followed by purification methods such as dialysis or repeated precipitations by salts, alcohol, acetone, etc., may be used, each preparation requiring special study in order to determine the best method of handling so that as much contaminating material as possible may be removed without at the same time causing inactivation of the enzyme.

Every enzyme preparation which has been obtained up to the present contains nitrogen. The amount present varies with the different enzymes, and also at times, for the same enzyme property, with the source and the method of preparation. The nitrogen content has been found to range from the very highly purified sucrase preparations [1] with 1.3%, to the amylase [2] and lipase [3] preparations which appear to consist essentially of protein matter (15% to 17% nitrogen). The nitrogen in all the

[1] J. M. Nelson and S. Born, *Jour. Amer. Chem. Soc. 36*, 393 (1914); H. Euler and O. Svanberg, *Z. physiol. Chem. 112*, 282 (1920).
[2] T. B. Osborne, *Jour. Amer. Chem. Soc. 17*, 587 (1895); H. C. Sherman and M. D. Schlesinger, *Jour. Amer. Chem. Soc. 34*, 1104 (1912), *37*, 643 (1915).
[3] K. G. Falk and K. Sugiura, *Jour. Amer. Chem. Soc. 38*, 921 (1916).

preparations studied was present in the form of protein and in every case as the usual nitrogenous constituents of proteins, without showing greater variations in these constituents than did proteins from other sources. The remaining constituents of enzyme preparations showed no specific characteristics, consisting in the different cases of carbohydrate complexes, fatty constituents, inorganic groups and elements, etc. In fact, it may be questioned whether the chemical compositions of the enzyme preparations as well as the colloidal properties do not represent merely the source of the enzyme material. At the same time it must be stated in this connection that attempts to obtain simpler enzyme bodies from the complex materials have resulted in almost all cases in destruction of the enzyme properties. This is not the place to enter into the question of the chemical structures of enzymes.[1] The purity of enzyme preparations, their chemical configurations, the changes in structure on inactivation, and similar questions, are of secondary importance for the present purpose. At the same time, the fact must not be lost sight of, that for a complete and satisfactory understanding of enzyme actions, whether considered as a group of catalytic actions or as ordinary chemical phenomena, a knowledge of the exact chemical composition and configuration of the enzyme, whether a complex molecule or one grouping of a complex molecule, is essential.

To return to the properties of enzymes, one of the most interesting of these and one which is being studied extensively is the change in activity with change in hydrogen ion concentration. It has been found that every enzyme action shows a maximum action at a more or less definite hydrogen ion concentration. In some cases this optimum is very sharp, in others it extends over a wide range. A list of these has been given elsewhere.[2] If the action of the hydrogen ion concentration were limited to enzyme actions, it might not be worth while to devote much space to it here. This is not the case, however. The hydrogen ion concentration of the medium for most reactions which take place in the liquid phase, either in solution, or between liquids, or between a solid or gas and a liquid, influences profoundly the reac-

[1] Cf. "The Chemistry of Enzyme Actions," Chapter VII, for a review of the recent work on this question.
[2] "The Chemistry of Enzyme Actions," pp. 65-6.

tions. This is observed so strikingly in certain reactions, that the hydrogen (or hydroxyl) ion has been assumed to be the predominating factor, even where it itself is not changed at the end of the reaction. The observed effects have been ascribed to the catalytic actions of these ions. Among the reactions which may be cited are the hydrolysis of sucrose (and other carbohydrates) by hydrogen ions, the hydrolysis of proteins by hydrogen or hydroxyl ions, the hydrolysis of esters by hydrogen or hydroxyl ions, etc. The interest in connection with enzymes is enhanced by the fact that these same reactions are the ones which have been studied most carefully from the point of view of the hydrogen ion concentration.

The catalytic actions of acids and bases (or of hydrogen and hydroxyl ions) have been treated in most text books as perhaps the best examples of catalytic actions which have been studied. The point of view adopted here is somewhat different. Emphasis is placed mainly on the chemical change which occurs, not on the unchanged factor (the catalyst) in the reaction.

The hydrolysis of sucrose was one of the earliest reactions for which accurate velocity determinations were made. In aqueous solution, the rate of reaction, as shown by the velocity constants, increases with increase in hydrogen ion concentration. Quantitative agreement is shown if the hydrogen ion concentration is small, but if it is high, the rate increases more rapidly than the hydrogen ion concentration. Hydroxyl ions do not appear to influence the reaction. The rate of change is negligible at moderate temperatures for very small hydrogen ion concentrations ($10^{-5.0}$N or less). The catalytic action is only observed therefore in solutions which are ordinarily considered to be acid. The action of the enzyme sucrase, at different hydrogen ion concentrations is in marked contrast to these actions. An optimum was observed at very nearly $[H^+] = 10^{-4.5}$ N for the sucrase preparations from yeast,[1] potatoes,[2], and bananas.[3] These preparations were inactive (as far as their sucrase actions were concerned) at $[H^+] = 10^{-2.5}$ N and $10^{-7.0}$ N. A sucrase preparation obtained from pneumococcus having an optimum ac-

[1] S. P. L. Sörensen, *Biochem. Z. 21,* 131 (1909); L. Michaelis and H. Davidsohn, *Biochem. Z. 35,* 386 (1911); H. A. Fales and J. M. Nelson, *Jour. Amer. Chem. Soc. 37,* 2769 (1915).
[2] G. McGuire and K. G. Falk, *J. Gen. Physiol. 2,* 215 (1920).
[3] G. McGuire and K. G. Falk, *J. Gen. Physiol. 3,* 595 (1921).

tion at $[H^+] = 10^{-7.0}$ N has been described,[1] while the optimum action for intestinal sucrase was found to be at $[H^+] = 10^{-6.8}$ N.[2] The hydrolysis of sucrose to form glucose and fructose is not a simple reaction. The complete reaction would include the formation of the α and β forms of glucose and fructose and the ethylene oxide and butylene oxide forms of the latter.[3] With acids, there are probably formed equilibrium mixtures of these different forms as the hydrolysis reactions proceed, the acids bringing about the equilibria rapidly; with sucrase, the reaction appears to proceed only to the formation of the α-glucose and α-fructose.

The quantitative results on the hydrolysis of proteins by acids and alkalies is rather scanty. A recent study[4] of this question has, however, supplied some of the desired data. Northrop followed the hydrolysis of gelatine at hydrogen ion concentrations between $10^{-0.5}$ N and 10^{-14} N at 25° and 40°. In strongly acid solution, $[H^+] = 10^{-2.0}$ N, the velocity of hydrolysis was proportional to the hydrogen ion concentration as determined by the hydrogen electrode. In strongly alkaline solution, $[H^+] = 10^{-10.0}$ N, the rate was proportional to the hydroxyl ion concentration determined similarly. The hydroxyl ions hydrolyzed the gelatine 30 times as rapidly as did the hydrogen ions at the same concentration. This should lead to a minimum rate of hydrolysis at about $[H^+] = 10^{-6.0}$N. Experimentally it was found that a minimum rate of hydrolysis occurred at this hydrogen ion concentration, but that the actual amount of hydrolysis was 300 times as great as that calculated on the assumption that the hydrogen and hydroxyl ions acted to the same proportionate extent as in the more acid and more alkaline solutions. Since there is no reason to assume that the hydrogen and hydroxyl ions have different properties or behave differently in the neighborhood of the neutral point than in the strongly acid or alkaline solutions, the explanation was advanced that a change in the gelatine occurred at the different ranges of hydrogen ion concentrations. A comparison of the deviation of the

[1] O. T. Avery and G. E. Cullen, *J. Exp. Med.* *32*, 583 (1920).

[2] H. Euler and O. Svanberg, *Z. physiol. Chem.* *115*, 43 (1921).

[3] Cf. "The Chemistry of Enzyme Actions," p. 44, for a summary of these relations.

[4] J. H. Northrop, *J. Gen. Physiol.* *3*, 715 (1921).

hydrolysis rate from that assuming proportionality of hydrogen and hydroxyl ion actions throughout, with the percent of uncombined gelatine present at the given hydrogen ion concentrations as shown by the titration curve for gelatine, led to the conclusion that the uncombined gelatine was hydrolyzed about 200 times as rapidly as the combined (or ionized), if the efficiency of the actions of the hydrogen and hydroxyl ions was the same both for the uncombined and combined gelatine. It was found that the hydrolysis of gelatine at constant hydrogen ion concentration obeyed the monomolecular reaction velocity law for about one-third of the reaction.

The effect of the hydrogen ion concentrations on the proteolytic enzymes (proteases) is apparently not so simple. As a matter of convenience, it has become customary, especially with enzyme actions, to indicate the hydrogen ion concentration by the symbol pH which represents the negative exponent of 10 (or the negative value of the logarithm to the base 10) of the number representing the hydrogen ion concentration. The following list gives a number of the values for the optimum hydrogen ion concentrations for the hydrolysis of proteins, usually at 37°, which are recorded in the literature.

	pH
Pepsin (edestin, casein)[1]	1.4
Pepsin (egg albumin)[2]	1.4
Pepsin (caseinogen, 10–15 min.)[3]	1.8
Pepsin (egg albumin, ½ to 1 hr.)[4]	1.6
Pepsin (egg albumin, 12 hrs.)[4]	1.2
Trypsin, pancreatic (albumose)[5]	7.7
Trypsin, pancreatic (casein)[6]	8.3
Trypsin, pancreatic (casein)[7]	5.5–6.3
Trypsin, pancreatic (fibrin)[7]	7.5–8.3
Erepsin, intestinal (albumose)[8]	7.7
Protease, yeast (peptides)[9]	6.8–8.5

[1] L. Michaelis and A. Mendelssohn, *Biochem. Z. 65*, 1 (1914).
[2] S. Okada, *Biochem. J. 10*, 126 (1916).
[3] L. Michaelis and H. Davidsohn, *Z. exp. Path. Therap. 8*, 398 (1910).
[4] S. P. L. Sörensen, *Biochem. Z. 21*, 131 (1909).
[5] L. Michaelis and H. Davidsohn, *Biochem. Z. 36*, 280 (1911).
[6] H. C. Sherman and D. E. Neun, *Jour. Amer. Chem. Soc. 38*, 2203 (1916); *40*, 1138 (1918).
[7] J. H. Long and M. Hull, *Jour. Amer. Chem. Soc. 39*, 1051 (1917).
[8] P. Rona and F. Arnheim, *Biochem. Z. 57*, 84 (1913).
[9] E. Abderhalden and A. Fodor, *Fermentforschung 1*, 533 (1916).

Protease, takadiastase (albumose)[1]	5.1
Pepsin, yeast (proteins)[2]	4.0–4.5
Trypsin, yeast (peptones)[2]	7.0
Erepsin, yeast (peptides)[2]	7.8
Pepsin, animal tissues (gelatine)[3]	3.0–3.5
Trypsin, animal tissues (peptone)[3]	7.8
Erepsin, animal tissues (glycylglycine)[3]	7.8
Papain (egg albumin, gelatine)[4]	5.0

There is no regularity apparent in these results. This is not so surprising when it is considered that the proteins which were used as substrates in most of this work were complex bodies of unknown compositions and structures, and that the enzyme preparations as well as the substrates were present in various stages of purity, or perhaps better with varying quantities of contaminating materials. Further, the hydrolysis of a protein involves decomposition of peptide linkings accompanied by the addition of the atoms of molecules of water. Peptide linkings of different resistance to decomposition exist in a protein molecule. The order in which these decompose may well be different under different conditions. For the present, it appears to be necessary to study a number of the individual reactions more thoroughly in order to obtain a general viewpoint and explanation. A definite beginning has been made by Northrop.[5] It was shown that the reaction between pepsin and a protein really occurs between ionized protein and free pepsin. "The optimum hydrogen ion concentration for the digestion of the protein must coincide with the hydrogen ion concentration at which the concentration of protein ions and therefore the conductivity due to the protein is at a maximum." The protein cations were obtained from the protein salt which was formed by adding acid to protein. After a certain amount had been added, further addition of acid would result in a decrease in the concentration of protein ions because of the increase in concentration of the common anion. A maximum concentration of protein ions would therefore result. "The limiting pH for the

[1] S. Okada, *Biochem. J. 10*, 130 (1916).
[2] K. G. Dernby, *Biochem. Z. 81*, 109 (1917).
[3] K. G. Dernby, *J. Biol. Chem. 35*, 179 (1918).
[4] E. M. Frankel, *J. Biol. Chem. 31*, 201 (1917).
[5] Cf. J. H. Northrop, *Science, 53*, 391 (1921), for a summary of this work together with references to the articles giving the experimental details.

activity of pepsin on the alkaline side must depend on the isoelectric point of the protein, since this is the point at which the protein first begins to react with the acid."

These conclusions mark a definite advance in the study of protease actions. Although the emphasis is placed principally upon the protein ion as such, it is probable that the structure or configuration of the protein molecule or complex which accompanies the formation of the protein salt, is responsible for the chemical action with pepsin as well as for the increased ionization. This point is of secondary importance at the present time and will unquestionably be cleared up in due course. The relations with the other protease actions have not as yet been followed similarly, so that it is impossible to go farther in this connection at present.

Northrop [1] also studied the mechanism of the hydrolysis of gelatine by acid, alkali, pepsin, and trypsin. It was found that: "1. Those linkages which are most rapidly split by pepsin or trypsin are among the more resistant to acid hydrolysis. 2. Those linkages which are hydrolyzed by pepsin are also hydrolyzed by trypsin. 3. Trypsin hydrolyzes linkages which are not attacked by pepsin. 4. Of the linkages which are hydrolyzed by both enzymes, those which are most rapidly hydrolyzed by pepsin are only slowly attacked by trypsin. 5. Those linkages which are attacked by trypsin or pepsin are among the ones first (most rapidly) hydrolyzed by alkali. In general it may be said that the course of the early stages of hydrolysis of gelatine is similar with alkali, trypsin, or pepsin and quite different with acid."

The hydrolysis of starch takes place in the presence of acid, and increases with increase in hydrogen ion concentration. The starch molecule is very complex, and in its decomposition a large number of products may be formed before the final product, glucose, is obtained. Thus, the following intermediate substances have been described, either in the breaking down of the starch by amylases or diastases or by acids: amylodextrin, erythrodextrin, achroodextrin, maltodextrin, maltose, glucose. In the enzymic decompositions of the starches, the following optimum hydrogen ion concentrations have been recorded:

[1] J. H. Northrop, *J. Gen. Physiol.* 4, 57 (1921).

	pH
Amylase, pancreatic [1]	7.
" malt [1]	4.4
" takadiastase [1]	4.8
" saliva [2]	6.
" potato [3]	6.–7.
" cabbage, carrot, white turnip [4]	6.
" yellow turnip [4]	4.–7.

The complex nature of the reaction makes the actual significance of these results somewhat uncertain. It is assumed by a number of chemists that the enzyme preparations which hydrolyze starch contain a number of different enzymes, and that each one of these enzymes takes part in only one step of the reactions involved in the decomposition of the starch. Evidence in favor of this view is seen in the fact that different results were obtained with amylase preparations acting upon soluble starch depending upon whether the amyloclastic (starch splitting, disappearance of blue color with iodine) or saccharogenic (formation of substances reducing cupric salts) actions were followed.[5] The latter refers to the amount of maltose (and glucose) produced, and the former to the amount of starch all of which is digested to a certain point within a certain time. In view of the complex natures of the substances involved and the reactions taking place, it will not be profitable to consider these reactions farther in the present connection.

The hydrolysis of esters and fats to form alcohols and acids has been studied extensively from various points of view. The behavior in solutions of different hydrogen and hydroxyl ion concentrations is similar to the behavior of the proteins. For equivalent concentrations, the hydroxyl ion exerted 1400 times as much action for the cases studied as the hydrogen ion.[6] In passing from an acid to an alkaline solution, a minimum action would be observed at about $[H^+] = 10^{-6}$ N, the velocity of reaction being greater in more acid and in more alkaline solutions.

[1] H. C. Sherman, A. W. Thomas, and M. E. Baldwin, *Jour. Amer. Chem. Soc. 41*, 231 (1919).
[2] R. V. Norris, *Biochem. J. 7*, 26, 622 (1913).
[3] G. McGuire and K. G. Falk, *J. Gen. Physiol. 2*, 215 (1920).
[4] K. G. Falk, G. McGuire, and E. Blount, *J. Biol. Chem. 38*, 229 (1919).
[5] H. C. Sherman and M. D. Schlesinger, *Jour. Amer. Chem. Soc. 35*, 1784 (1913).
[6] J. J. A. Wijs, *Z. physik. Chem. 11*, 492; *12*, 514 (1893).

The velocities run parallel to the increase in hydrogen and hydroxyl ion concentrations, but, except for limited ranges, are not strictly proportional. Considerable work has been done on the mechanism of these reactions, and much evidence brought forward to prove the existence of intermediate compounds.[1] The unstable nature of these intermediate products and the consequent difficulty attending their isolation, have obscured the course of the reaction. On the other hand, the work of Stieglitz on the imido esters, to which reference has been made before in this book, has thrown much light on the mechanism of such reactions. The hydrolysis of the imido esters by the addition of acids was shown to be due to the increased concentration of one of the reacting species (ester ion in this case) and the relations were interpreted according to well-known chemical laws. The compounds formed in the different stages of the reactions were isolated and identified, and the reactions, as well as a number of analogous reactions, were removed from the mysterious realms of catalytic actions and interpreted according to simple chemical principles. Imido esters were studied in place of ordinary esters because of the greater ease of following the reactions experimentally, but the general conclusion arrived at, that the increased reaction velocity was due to the increased concentration of the reacting constituents is unquestionably true for the increased hydrolysis of esters because of the presence of hydrogen and hydroxyl ions, and the natures of the intermediate compounds in the two series are probably similar.

The optimum hydrogen ion concentrations for the enzymic hydrolysis of esters and fats have been determined in a few cases. The results were as follows:

	pH
Esterase, pancreatic[2]	8.3–9.
Esterase, blood serum[2]	8.
Lipase, duodenal juice[3]	8.5
Lipase, gastric juice[3]	4. –5.

[1] Cf. K. G. Falk and J. M. Nelson, *Jour. Amer. Chem. Soc.* 37, 1732 (1915), for references to the experimental evidence regarding the existence of these compounds; also G. Baume and G.-P. Pamfil, *J. chim. phys.* 12, 260 (1914); J. Kendall and co-workers, *Jour. Amer. Chem. Soc.* 36, 1222, 1722, 2498 (1914); 37, 149 (1915); 43, 1426 (1921).

[2] P. Rona and Z. Bien, *Biochem. Z.* 59, 100; 64, 13 (1914).

[3] H. Davidsohn, *Biochem Z.* 49, 249 (1913).

The reactions here are simpler than with the hydrolysis of the proteins. The chemical compositions and structures of the initial and final products of the reaction (that is to say, of the substances which are changed) are known. The difficulty of studying this problem is of a different sort. The enzymic activity of esterase and lipase preparations is lost comparatively rapidly as a rule, even on simple treatments. This makes it difficult to prepare highly active preparations and to remove inactive materials. The interesting result of the determinations of optimum hydrogen ion concentration conditions here, as with the protease preparations, is to be found in the fact that the maximum actions in the presence of enzymes were obtained at the hydrogen ion concentration where, in the absence of the enzymes, the actions approached a minimum.

The results involving the effects of different hydrogen ion concentrations on the velocity of these chemical reactions in the absence and in the presence of enzymes, appear to indicate that the reactions in the two series are fundamentally different. If attention is fixed upon the actual chemical change taking place, there is no fundamental difference observable, although apparent differences are seen because a reaction may have proceeded farther (or several successive stages may have occurred) in one case than in another. The hydrogen ion (or the hydroxyl ion) and the enzyme are present after the reaction, presumably as far as can be told, as the same compound as before (some secondary changes will be spoken of presently). Either from this point of view, or from the point of view of change in reaction velocity, both the hydrogen ion (or hydroxyl ion) and the enzyme would be grouped as catalysts, and the reactions included under catalytic changes. The evidence available in the few cases where quantitative studies have been carried out, indicates that the course of the changes includes the formation of intermediate compounds or that the reactions take place in stages. Evidence for, and deductions from, this general view of the mechanism of chemical reactions, has been presented elsewhere [1] in some detail.

The relations existing between the hydrogen ion concentration of the medium, whether or not enzyme is present, and the velocity of the corresponding chemical reaction are so compli-

[1] "Chemical Reactions; Their Theory and Mechanism."

cated, or at any rate have not been explained in many cases, that it does not appear advisable to devote much space to conditions under which these reactions take place where, in addition, certain substances are added which influence the velocities. The general viewpoint or theoretical significance of these relations is unsatisfactory, and it will only be possible to group them in a more or less superficial manner. With regard to the reactions taking place in the absence of enzymes, it has been found that neutral salts change the velocities with highly ionized acids, in ways which cannot be accounted for on the basis of decreased ionization of the acids. The hydrolysis of sucrose and of esters has been studied in this way. The view called the "Dual Theory of Catalysis" was developed, in which the unionized acid molecule as well as the hydrogen ion was assumed to act as catalyst.[1] The next step which was taken considered ionization as secondary to some change in the medium involving primarily the solvent. According to this view, chemical action and ionization represented chemical and physical evidences, which paralleled each other in some cases and not in others, of this more deep seated relation.[2] It may be stated, however, that no theory of these phenomena has been generally accepted up to the present time, although their importance in catalytic reactions is universally recognized.

It is obvious that with enzyme actions the phenomena are still more complicated. The behaviors of the enzyme preparations and the changes these may undergo, entirely aside from the influence on chemical reactions upon which they may be said to exert catalytic actions, must be considered carefully. In a sense, it is impossible to separate the properties of enzymes from the chemical reactions which they influence, since enzyme actions are known only because of these influences.

In the first place, enzyme preparations lose their activity under comparatively simple conditions, a result which at times

[1] Cf. the summary in W. C. McC. Lewis, "A System of Physical Chemistry," 1918, Part I, pp. 423-9. The historical development of the views is of interest, but can only be referred to here. For example, the first suggestion of the possible activity of unionized molecules in catalytic actions by H. Goldschmidt in 1899 (*Z. physik. Chem.* *19*, 118); the increasing importance ascribed to the simultaneous actions of unionized molecules and of hydrogen ions by J. Stieglitz (*Am. Chem. J.* *39*, 167 (1908)), S. F. Acree and J. M. Johnson (*Am. Chem. J.* *37*, 410 (1907); *38*, 329 (1908)), and others, etc., may be mentioned.

[2] K. G. Falk and J. M. Nelson, *Jour. Amer. Chem. Soc.* *37*, 1732 (1915); K. G. Falk, "The Chemistry of Enzyme Actions," pp. 48-53.

brings out the similarity between enzyme actions and life processes in a striking manner. When enzyme preparations are heated in solution, at first the enzyme actions are increased (as with all chemical reactions) up to a maximum generally in the neighborhood of 38°, and then, at higher temperatures, the activities are lost. This is the general phenomenon as observed, but it is best interpreted by considering that loss of activity occurs even at moderate temperatures, that there is a balance between this loss and the increased activity due to increased temperature, that a maximum activity is obtained at a certain temperature, and that finally the loss predominates until inactivation is complete. The conditions of the environment, such as acidity of medium, etc., are also involved in the rate of inactivation by temperature. Some enzymes are more resistant to heat than others, so that no general statement with regard to this phenomenon is possible, except that the inactivation is connected with a chemical change involving the enzymic molecular structure or grouping.

The differences in activity of enzyme preparations at different hydrogen ion concentrations is a striking feature of enzyme actions. It is necessary apparently for the enzyme molecule or grouping to possess a definite state, configuration, or structure in order to show the requisite behavior. Another factor is involved, however, but can be disposed of briefly. The activity of all enzyme preparations can be destroyed permanently by treatment with acid or alkali of sufficient strength. The concentration of hydrogen or hydroxyl ions necessary for this irreversible inactivation varies with the enzyme, with accompanying inactive material, with temperature, and with time of action. Since so many factors may be involved, it will not be advisable to enter into a detailed discussion of this question here except to point out that the change is unquestionably one involving change in internal structure of the active enzyme molecule or grouping, because of the very mild acid or alkaline treatments which frequently bring about this inactivation. The reversible partial inactivation may also be due to change in internal structure of the enzyme molecule or grouping. Attempts have been made to determine whether the activity was connected with or part of the unionized molecule or one of the ions. Experiments

showing the direction of migration in solution in an electric field have answered this question for a number of enzymes. Michaelis [1] gave the following summary of the results which had been obtained: with sucrase, the unionized molecule contained the active enzyme; with trypsin, erepsin, lipase, and maltase, the anions were active. With pepsin, the cations appeared to be active, but further careful work showed that with a preparation of purified pepsin no migration in an electric field occurred, and only when a protein (albumin or albumose) was added did migration take place with the protein.[2] The reversible inactivation of enzymes is probably connected with reversible changes, perhaps of a tautomeric nature, within the molecule containing the enzyme, and the ionization properties parallel these changes in some cases without being responsible directly for the enzyme actions. It must also be recalled that the differences in hydrogen ion concentrations may affect the structure of the substrate as well as of the enzyme. This was shown in the action of protease by Northrop, who found that it was necessary for the protein which was acted upon by pepsin to be in an ionized state, and by Long and Hull,[3] who stated that the optimum hydrogen ion concentration for the action of pancreatic trypsin on casein was given by the value of pH 5.5–6.3, and on fibrin of 7.5–8.3. It is possible that this view is of much wider applicability, that in addition to the condition of the substrate in enzyme actions being one of the determining factors, it is also necessary for the substances which are transformed to possess certain definite structures in chemical reactions involving catalysts not enzymes. In a sense, this is a generalized statement of the phenomena described by Stieglitz in his imido ester work where either the formation of a new substance, or increasing the concentration of a substance present only in minimal quantities before the addition of the so-called catalyst, resulted in the speeding up of the chemical change. The imido ester ion in the work of Stieglitz was the main reacting substance after the addition of acid to imido ester. The compositions and structures of these substances are known and are comparatively simple. At the same time, there appears to be no reason why this view should not be

[1] L. Michaelis, *Biochem. Z. 60*, 91 (1914).
[2] C. A. Pekelharing and W. E. Ringer, *Z. physiol. Chem. 75*, 282 (1911).
[3] J. H. Long and M. Hull, *Jour. Amer. Chem. Soc. 39*, 1051 (1917).

extended to more complex substances and also to substances or mixtures where the various intermediate products are too unstable to have been isolated.

Neutral salts increase the velocity of hydrolysis of sucrose and of esters by highly ionized acids. This is explained on the basis of the Dual Theory of Catalysis by considering that the neutral salt decreased the degree of ionization of the acid and since the acid molecule exerted a greater action than the hydrogen ion, the velocity of the reaction was increased. This view depends upon certain assumptions relative to the degrees of ionization of the electrolytes. There has been considerable work done, especially in recent years, on this question, and a number of papers published in which the view was advocated that for strong electrolytes ionization was complete, and that the observed and calculated values obtained for the percentages of ionization show deviations from the values for complete ionization because of secondary relations.[1] This view, if correct, obviously would require modification of the Dual Theory of Catalysis. At the same time, it may be pointed out that on the addition theory of chemical reactions, as presented in another connection,[2] ionization is a secondary phenomenon, and the reactions are accounted for on the basis of the formation of intermediate addition compounds.

The actions of neutral salts on enzymes may be extended to include the actions of a large number of organic as well as inorganic substances which in one way or another modify the rate of change of the reaction in which the enzyme is involved. The general problem was seen to be in an uncertain state in considering the reactions in the absence of enzymes and in the presence of such a chemically simple catalyst as the hydrogen ion. There is no explanation of the observed facts which has as yet found general acceptance. It is obvious, then, that in enzyme actions, where the possibility exists of the neutral salt

[1] W. Sutherland, *Phil. Mag.* (6) *14*, 3 (1907); S. R. Milner, *Phil. Mag.* (6) *35*, 214, 354 (1918); J. C. Ghosh, *J. Chem. Soc. 113*, 449, 627 (1918); N. Bjerrum, *Z. Elektrochem. 24*, 321 (1918); A. A. Noyes and D. MacInnes, *Proc. Nat. Acad. Sci. 6*, 18 (1920); *Jour. Amer. Chem. Soc. 42*, 239 (1920); J. C. Ghosh, *Z. physik. Chem. 98*, 211 (1921); G. Akerlöf, *Z. physik. Chem. 98*, 260 (1921); H. Kallman, *Z. physik. Chem. 98*, 433 (1921); R. H. Clark, *Jour. Amer. Chem. Soc. 43*, 1759 (1921); L. Ebert, *Jahrb. Radioaktiv. Elektronik 18*, 134 (1921).

[2] "The Chemistry of Enzyme Actions," pp. 49, 51.

or other added substance acting, not only upon the chemical change which is being followed, but also upon an enzyme substance of unknown complexity and composition as a rule, but readily modified by external agencies, the theoretical interpretation of the experimental facts observed will be still less satisfactory. As indicated, an added substance may produce an effect by acting upon the substrate or upon the enzyme. It has been found that many substances produce such actions, a number increasing the velocities of the enzyme actions, others decreasing the velocities. A considerable literature has grown up around these phenomena, such names as activators, co-enzymes, anti-enzymes, etc., being used to denote the substances or mixtures producing these actions. Regularities have been observed with certain series of salts on various enzyme actions. The whole question is at present at the empirical stage. Much of the data is not useful, because conditions of experimentation were not sufficiently controlled. Thus, the hydrogen ion concentration of a mixture must be kept constant if a series of neutral salts is studied; the formation of precipitates must be considered in carrying out enzyme tests; etc. Altogether, it is impossible at present to give a general viewpoint in connection with these actions and this is not the place to enumerate the many changes which have been observed and recorded. One line of work may, however, be mentioned. Certain substances exert such unique effects upon the velocities of definite enzyme actions that it appears as if these effects would prove to be the most direct ways of obtaining knowledge of the changes involved, of the conditions which make such changes possible, and possibly of the chemical nature of the enzymes themselves. For example, reference may be made to the large increases in velocities produced by hydrogen cyanide on the proteolytic enzyme papain,[1] by bromide (as distinct from chloride and iodide) on amylase,[2] by manganous sulfate on castor bean lipase,[3] etc.

Before leaving this part of the subject, it may be mentioned that, in addition to the reactions cited because of their impor-

[1] E. M. Frankel, *J. Biol. Chem. 31*, 201 (1917); cf. also H. S. Vines, *Ann. Bot. 17*, 606 (1903); L. B. Mendel and A. F. Blood, *J. Biol. Chem. 8*, 177 (1910).
[2] A. W. Thomas, *Jour. Amer. Chem. Soc. 39*, 1501 (1917).
[3] E. Hoyer, *Z. physiol. Chem. 50*, 414 (1907); Y. Tanaka, *Orig. Com. 8th Intern. Congr. Appl. Chem. 11*, 37 (1912); K. G. Falk and M. L. Hamlin, *Jour. Amer. Chem. Soc. 35*, 210 (1913).

tance in enzyme actions, the velocities of many chemical reactions may be greatly increased by the addition of more than one "catalyst." Thus one of the most interesting examples which has attained considerable importance in recent years involves the oxidation of carbon monoxide. At ordinary temperatures, this reaction is extremely slow, if it can be said to take place at all. The study of a number of oxides showed that in the presence of a mixture of the four oxides, MnO_2 (50%), CaO (30%), Co_2O_3 (15%), and Ag_2O (5%), carbon monoxide was oxidized rapidly by the oxygen of the air at ordinary temperatures.[1] Further examples of such actions will be given in Chapter VIII, but it may be stated here that satisfactory explanations or reasons for the greater actions of mixtures of several substances as compared with the action of a single substance, are lacking.

One of the most interesting features of enzyme actions which has frequently been referred to as characteristic of such actions is the specificity. A certain enzyme preparation acts upon one reaction or group of reactions and not upon other reactions. The enzyme sucrase hydrolyzes sucrose (and probably raffinose) and not maltose; maltase hydrolyzes maltose and not sucrose; castor bean esterase and lipase preparations both hydrolyze simple esters and glycerides, but to different extents; the various proteases are limited in their actions upon proteins, but the different ones, pepsin, trypsin, and erepsin, hydrolyze proteins or their partial decomposition products to different extents and under different conditions; urease hydrolyzes urea rapidly and methyl urea only slightly if at all; etc. This question was discussed in some detail in another connection.[2] "These specificities are striking in many cases, but not unique considered as chemical phenomena. The most obvious reactions in which specificities are used are those included in Qualitative Chemical Analysis (and also Quantitative Analysis). In the reactions involving the identification of the metallic elements, these may be compared to the substrates in enzyme actions, and the reagents used to enzyme preparations or materials. There are, in both cases,

[1] A. B. Lamb, W. C. Bray and J. C. W. Frazer, *J. Ind. Eng. Chem.* **12**, 213 (1920).

[2] "The Chemistry of Enzyme Actions," pp. 127-8. An example of such an action was published recently by E. Abderhalden and H. Handovsky (*Fermentforschung* **4**, 316 (1921)). They found that yeast juice hydrolyzed glycyl-*l*-eucylglycyl-*l*-leucine but not glycyl-*d*-leucylglycyl-*l*-leucine.

group reagents and individual reagents. With enzymes, for example, amylase, different proteases, emulsin, lipase, etc., act upon certain groups of substances. Within each group there will be smaller differences for each individual substrate with the group reagent. The conditions must also be kept within certain limits. In qualitative analysis, similarly, hydrogen sulfide might be used as an example of a reagent showing group reactions with certain metallic elements in solution, as well as differences with the individuals in the group, while the conditions of the reaction (such as acidity or alkalinity, etc.) must be kept within certain limits. These analogies might be multiplied indefinitely. One set of phenomena is as remarkable as the other, but familiarity with the one has made these reactions commonplace, while the practical necessity for replacing definite chemical substances by substances as yet not as well characterized and therefore known by names less familiar has resulted in enzyme actions and their specificities acquiring a certain air of mystery. This is unjustified, and their reactions are no more mysterious than are other chemical reactions."

Of similar tenure is the conclusion of Northrop, who stated, as a result of the study of the comparative hydrolysis of gelatin by pepsin, trypsin, acid, and alkali, to which reference was made earlier in this chapter that "There does not seem to be any evidence to distinguish qualitatively between the specificity of an enzyme and of hydrogen ions." [1]

The substances upon which many enzymes exert their actions are frequently of complex nature. The products formed partake often of some of the characteristics of the initial substrates. Since action occurs between enzyme and substrate, it is not surprising that action may also occur between enzyme and products. The former manifests itself by an increase in the velocity of the chemical reaction, the latter by a modification of this increase. Michaelis and Menten [2] showed that the action of sucrase was inhibited by the products of the reaction it influenced. Fructose retarded the actions much more markedly than did glucose. These facts have been confirmed and extended in various directions in recent years by J. M. Nelson and his co-

[1] J. H. Northrop, *J. Gen. Physiol.* *4*, 57 (1921).
[2] L. Michaelis and M. L. Menten, *Biochem. Z.* *49*, 333 (1913).

workers. The explanation advanced for this retardation is based upon the formation of chemical compounds of the sucrase with glucose and fructose. In this way the sucrase is removed from the sphere of action and is unable to react farther with the sucrose. The greater retardation shown by the fructose in comparison with the glucose, points to chemical phenomena as involved in the combinations. Similar retardations of enzyme actions by the products of the decomposition of the substrate have been observed in the action of amylase on starch in which maltose exerted a retarding influence [1] and in the action of pepsin on protein in which peptone or albumose caused the retardation.[2] A somewhat different type is the irreversible inhibiting action of the products of an enzyme action as shown in the action of benzaldehyde on emulsin and probably also of simple alcohols (not glycerin) on esterases.[3] These phenomena are evidently special cases of the retarding actions of certain substances on enzyme actions, simpler in the sense that no foreign substance is added initially. They are explained, as stated, by those who have studied the reactions, as due to combination of one or more of the products with the enzyme substance, in that way removing the enzyme from the sphere of action. In some cases, the combination is followed by precipitation. Such actions as change in hydrogen ion concentration of the medium by the products of the reaction are not directly included in these relations, but even these may be considered from the same point of view, the acid or alkali produced combining with the enzyme. In this way, the hydrogen ion concentration of the solution may well be changed, this change being accompanied by a change in internal structure of the enzyme molecule. The three phenomena brought about by acid or alkali; combination with the acid or alkali, change in structure of the enzyme grouping or molecule, and change in activity, appear to run parallel.

The question of the mathematical formulation of the kinetics of enzyme actions may be considered briefly.[4] It has been pointed out that the mathematical formulation of the velocities

[1] A. Wohl and E. Glimm, *Biochem. Z.* **27**, 349 (1910); G. McGuire and K. G. Falk, *J. Gen. Physiol.* **2**, 224 (1920).
[2] J. H. Northrop, *J. Gen. Physiol.* **2**, 471 (1920).
[3] K. G. Falk, *Jour. Amer. Chem. Soc.* **35**, 616 (1913).
[4] A summary of some of these relations, especially as bearing upon the question of pepsin action, was given by J. H. Northrop, *Science* **53**, 391 (1921).

of chemical reactions and changes in these velocities due to added substances has not proven satisfactory, and that various attempts have been and are being made to reconstruct the hypotheses upon which the formulations are based. It is evident that the introduction of another factor, such as the enzyme, may increase the difficulties involved in the formulations. These increased difficulties will not be gone into here; but, on the other hand, some of the properties peculiar to enzymes and their actions have made it possible to indicate and make probable from a somewhat different angle a possible solution of some of the questions involved.

In an enzyme action, the rate of reaction is found to be proportional to the enzyme concentration in some cases but not in others. This proportionality can only be said to hold within certain limits of concentration of enzyme substance and substrate. The interference due to the products of the reaction, the presence of other substances, the necessity in many cases of having both the enzyme and substrate in a given condition as evidenced by the hydrogen ion concentration optimum, all may play a part here. Also, the fact that the reactions in all probability take place in several stages, as will be elaborated presently, undoubtedly complicates the question. It has also been found experimentally that with a number of enzymes, the amount of action is proportional to the square root of the enzyme concentration (Schütz's rule).

With regard to the change in substrate concentration, with a given enzyme concentration and dilute substrate concentration the action is proportional to the substrate concentration as a rule. With increasing substrate concentration, the increase in action is less rapid, and with a number of enzymes, after a certain concentration has been reached, the action is not increased by more substrate. In other words, there appears to be a maximum capacity of an enzyme preparation for hydrolyzing a substrate, no matter how much excess substrate may be present above a certain quantity. This relation has been found to hold for the following enzyme actions: Sucrase, sucrose;[1]

[1] A. Brown, *J. Chem. Soc. 81*, 373 (1902); E. Duclaux, Traite de Microbiologie, Tome II, Diastases, Toxines, et Venims, Paris (1899); L. Michaelis and M. L. Menten, *Biochem. Z. 49*, 333 (1913); J. M. Nelson and W. C. Vosburgh, *Jour. Amer. Chem. Soc. 39*, 790 (1917).

amylase, starch;[1] lactase, lactose;[2] maltase, maltose;[2] emulsin, glucosides;[2] lipase, esters;[3] urease, urea.[4] These results can be accounted for most readily on the intermediate compound theory, each enzyme showing a maximum capacity for combination with the substrate, if the latter is present in large excess. The rate of reaction will then be proportional to the concentration of the addition compound of enzyme and substrate if its decomposition is slower than its formation and a steady state will then exist with regard to the combined condition of the enzyme. Either all of the enzyme, or a constant fraction of it, will exist all the time combined with the substrate. This relation, obviously, will hold only as long as no interfering actions such as may be caused by the products of the reaction, etc., occur.

The question of Schütz's rule may be considered as an example of the modifications in the mathematical deductions made necessary at times by complex experimental conditions. Schütz[5] found experimentally that in the action of pepsin on egg albumin, the amounts of egg albumin digested (to peptone) in a given time with different quantities of pepsin were proportional to the square roots of the concentrations of pepsin. This rule was found to hold for the first part (one-third to one-half) of the reaction by different workers. Also, the rule was found to hold for different enzymes, including lipase and diastase, under certain conditions.

Arrhenius[6] showed that in the hydrolysis of ethyl acetate present in great excess, by ammonia (or ammonium hydroxide), the mathematical equation representing the change was analogous to the equation of Schütz's rule after the first moments of the reaction. The ammonium ion of the ammonium acetate formed in the reaction repressed the ionization of the ammonium hydroxide and therefore the concentration of the hydroxyl ions. The velocity would be inversely proportional to the amount of

[1] H. T. Brown and T. A. Glendinning, *J. Chem. Soc. 81*, 388 (1902); C. L. Evans, *J. Physiol. 44*, 191 (1912).
[2] E. F. Armstrong, *Proc. Roy. Soc. London (B), 73*, 500 (1914).
[3] H. C. Bradley, *J. Biol. Chem. 8*, 251 (1910); G. Peirce, *Jour. Amer. Chem. Soc. 32*, 1517 (1910); K. G. Falk and K. Sugiura, *Jour. Amer. Chem. Soc. 37*, 217 (1915).
[4] D. D. van Slyke and G. E. Cullen, *J. Biol. Chem. 19*, 141 (1914).
[5] A summary together with many references is given by H. Euler, "Allgemeine Chemie der Enzyme," 1910, pp. 127-137.
[6] S. A. Arrhenius, Medd. Kong. vetsakad. Nobelinst. (1908) 1,

ammonium acetate formed after the first few minutes of the reaction. The following general equation was deduced:

$$A \log_e \frac{A}{A-x} - x = kqt \qquad (1)$$

in which A represents the concentration of ammonia at the beginning of the reaction, x the quantity transformed into ammonium acetate at the time t, q, the concentration of ester, and k the reaction velocity constant. Before x becomes too large (as with the enzyme actions just mentioned) this equation reduces to the form

$$x = \sqrt{kAqt} \qquad (2)$$

which is an expression of Schütz's rule, and which was found to hold for the hydrolysis of ethyl acetate by ammonia under the indicated conditions.

A more exact equation apparently similar in form to the equation of Arrhenius was deduced by Northrop [1] in connection with the study of the digestion of proteins by pepsin in order to represent the complete course of the reaction. The action was shown to be caused by free pepsin, and the amount of free pepsin, after the first few minutes was found to be inversely proportional to the amount of products. The pepsin was present in solution free or in combination with the products of hydrolysis of the protein, the relative concentrations following the law of mass action. The equation of Northrop is as follows:

$$q \log_e \frac{q}{q-x} - x = kEt \qquad (3)$$

E representing the concentration of enzyme. The equation differs from that of Arrhenius in that in the latter the substrate concentration was assumed to remain constant while the enzyme concentration was represented by the term $(A-x)/x$, and in the former, the substrate concentration was expressed by the term $q-x$, and the enzyme concentration by the term

[1] J. H. Northrop, *J. Gen. Physiol.* **2**, 471 (1920).

E/x. Neither the Arrhenius nor the Northrop equation represents the experimental facts for the first few minutes of the reaction (until the concentration of substrate decomposed is large, ten to fifteen times as great as the concentration of active pepsin). Both equations simplify to Schütz's rule for the next thirty to forty per cent of the reaction, and after that, when the substrate is no longer present in great excess and its concentration can no longer be considered constant in the mathematical formulation, the Northrop equation more nearly represents the experimental facts.

These deductions strictly speaking apply only to the pepsin-protein reaction. The general method of treatment should, however, be applicable as well to other enzyme actions, but only after these have been subjected to similar careful experimental study.

In every discussion of chemical reaction velocity, the question of the reaction in the opposite direction, or the reversibility of the reaction, must be considered. It has been found experimentally that a number of enzyme preparations, including lipase, emulsin, trypsin, pepsin, kephirlactase, maltase, and oxynitrilase, bring about syntheses of more complex bodies from the simpler substances which were produced by the actions of the same or similar preparations.[1] Quantitative work unfortunately is not available relative to the synthetic actions of these enzyme preparations, comparable to their decomposing actions. The possible effect of the presence of an enzyme on the equilibrium concentrations of the reacting constituents has also not been subjected to careful study as yet.

The phenomena of enzyme reactions which have been described briefly and rather superficially in the last pages can be brought together so as to indicate, in part at any rate, the mechanism of the changes and at the same time emphasize again the fact that enzyme actions belong to the group of catalytic actions, and to show as well their relations to chemical reactions in general. The following scheme of equations represents some of the possible actions in a complex mixture such as might occur in an enzyme action:

[1] For references, cf. "The Chemistry of Enzyme Actions," pp. 104-5.

$$\left[\begin{array}{l}\text{Enzyme}\\ \text{Substrate}\\ \text{(or Products)}\\ \text{Water}\end{array}\right] \begin{array}{ll}= \text{Enz.} + \text{Substr.} + \text{Water} & \text{(a)}\\ = \text{Enz.} + \text{Products} + \text{Water} & \text{(b)}\\ = (\text{Enz. Products}) + \text{Water} & \text{(c)}\\ = (\text{Enz. Substrate}) + \text{Water} & \text{(d)}\end{array} \quad (4)$$

These equations do not show the actions of any other substances, and, in fact, outline only the simplest changes which can take place for enzyme actions involving hydrolysis reactions. An analogous set of equations would be necessary to represent oxidation-reduction reactions. This set of equations is similar in form to the equations which were given in a previous chapter to represent the mechanism of chemical actions.

Starting with the substances on the right hand side of equation (a), if the products of equation (b) are obtained, the simplest case of enzyme action would be represented. Here, as in all examples of chemical kinetics, if a reaction takes place in two (or more) stages, the reaction which has the smaller rate is the one to be measured experimentally, if the difference in rates is sufficiently great. If this difference is not large enough, uncertain and confusing results may be obtained in the application of the (simplified) mathematical formulas to the chemical equations which may represent only a part of the chemical changes actually taking place. With certain simplified conditions, such as the presence of a large excess of substrate, simplified mathematical expressions will be found to hold. In such a case, the reaction velocity measured is, as a rule, the decomposition rate of the intermediate addition compound, equation (b), since the reaction represented by equation (a) has assumed a steady state which can be deduced from the mass action relations as indicated by Northrop for a special case. Another factor which makes the application of the kinetic equations uncertain at times is the physical condition of the enzyme preparation and the substrate. The enzyme preparation is almost always colloidal in character, while the substrate may also be a colloid as with proteins, starches, and some fats. The ordinary application of the mass action expression may be open to question here, because of the difficulty of determining the active mass of the colloidal particle. The introduction of the concentration as the active mass does not appear warranted without further direct evidence.

This general question was discussed in an earlier chapter and will be taken up again under "Contact Catalysis" in Chapter VIII. At the same time, it may be mentioned that experiments showed a sucrase preparation not to be affected in its activity whether or not the enzyme was adsorbed on a solid like charcoal, or on a colloid like saponin, serum, or egg albumin, or distributed uniformly throughout the solution of the substrate;[1] that with pepsin, the state of aggregation of the protein, whether in solution or not, exerted no marked influence on the rate of digestion;[2] and that with a castor bean lipase preparation, whether the enzyme material was dissolved in salt solution or suspended in the aqueous solution, appeared to make little or no difference in its hydrolyzing action.[3]

Equation (c) in the general formulation represents the possible interference due to the enzyme combination with the products of the decomposition of the substrate. Obviously it is not necessary for the reaction between the products and the enzyme, or the equilibrium between them, to pass through or include the intermediate addition compound. An equation including these alone might be written, but for the sake of showing the general relationship, this has not been done. Similarly, equation (d) shows the combination of enzyme and substrate. That such combinations exist and play an important part at times may be illustrated by the fact that a number of enzyme preparations have been found to be more resistant to factors which cause inactivation in the presence of their substrates than in their absence. This has been found to be true, for example, for sucrase,[4] trypsin,[5] and amylase.[6]

The significance of the enzyme term in the equations requires some explanation. The exact concentration to be used in the kinetic and other formulations must be determined for each individual action. The hydrogen ion concentration of the me-

[1] J. M. Nelson and E. G. Griffin, *Jour. Amer. Chem. Soc. 38*, 1109 (1916); cf. also J. M. Nelson and D. I. Hitchcock, *Jour. Amer. Chem. Soc. 43*, 1956 (1921).

[2] J. H. Northrop, *J. Gen. Physiol. 1*, 607 (1919); W. E. Ringer, *Z. physiol. Chem. 95*, 195 (1915).

[3] K. G. Falk, *Jour. Amer. Chem. Soc. 37*, 226 (1915).

[4] C. O'Sullivan and F. W. Tompson, *J. Chem. Soc. 57*, 834 (1890).

[5] W. M. Bayliss and E. H. Starling, *J. Physiol. 30*, 61 (1903); cf. also W. M. Bayliss, *Proc. Roy. Soc. London (B) 84*, 81 (1911).

[6] T. B. Osborne and G. F. Campbell, *Jour. Amer. Chem. Soc. 18*, 536 (1896); H. C. Sherman and co-workers, series of papers in *Jour. Amer. Chem. Soc.* 1914-1921.

dium is naturally the first factor to be thought of in this connection, because of the optimum conditions which have been found to exist for all enzyme actions. Similarly there may be optimum conditions for the substrate, as with the protein ions which Northrop showed were essential for optimum pepsin action. Also, there may be optimum conditions for the decomposition of the intermediate addition compound which may be different from the optimum conditions for its formation.

The actions of foreign substances, foreign in the sense that they are not involved in the simplest formulations of the reactions, may exert considerable influence. Thus, they may combine with the enzyme, a reaction similar to equation (c) of the general formulation, in a reversible or irreversible way, and remove it from the sphere of action; they may combine with the products of the reaction, and by removing them favor the enzymic decomposition; they may combine with the substrate, or cause a change in it which would interfere with the reaction; etc. In every case, however, the interpretation of the reaction is a chemical one. The changes are analogous to changes in ordinary, well-known chemical reactions. The exact chemical formulas and structures cannot be given here and recourse must be had, temporarily it is to be hoped, to more or less definite symbols. With these limitations in mind, the application of the ordinary chemical laws and theories may be carried out in exactly the same way as with chemical reactions involving substances of simpler compositions and structures.

In this chapter a brief review of enzyme actions considered as a group of catalytic actions was presented. Many of the chemical changes included in enzyme actions may also be brought about by hydrogen and hydroxyl ions, or perhaps better, may involve these ions. The actions of hydrogen and hydroxyl ions were therefore included in the discussions in this chapter, but not with the intention of belittling their importance and significance by apparently considering them incidentally. Their actions have been treated in detail in various publications by a number of workers. Unfortunately, definite conclusions have not been reached in comparatively simple reactions such as the hydrolysis of sucrose or of esters by these ions. In fact, the determination of the degree of ionization has not been satisfactorily elucidated

so as to make possible the development of a general viewpoint. On the other hand, the work of Stieglitz on the decomposition of imido esters and related compounds does give a definite viewpoint from which to consider the so-called "catalytic" actions of hydrogen ions and brings these actions into line with chemical reactions in general. His general theoretical conceptions may be carried over to reactions such as the hydrolysis of esters. Chemical evidence is at hand to bear out a number of the deductions but the exact formulation of the changes to be included in such reactions as the hydrolysis of esters is not certain even under these conditions. It was considered advisable therefore to omit the detailed discussion of these reactions in the present connection. Enzyme actions being of more complex nature offer more points of contact with other branches of chemistry and related sciences and indicate possibilities of development, some of which will be considered in the following chapter. The present chapter was therefore headed "Enzyme Actions" and hydrogen and hydroxyl ion actions considered briefly in the discussion of the chemical changes involved. At some other time and in some other connection it is possible that the interests of the writer will be shifted so that a chapter such as this would be headed "Hydrogen and Hydroxyl Ion Actions" and enzyme actions considered in connection with these. The actions of other ions or molecules might also be considered as the dominant actions. In any given case, the personal preference, at the time, of the one presenting the subject will be the decisive factor in the method of treatment to be followed.

Chapter VII.

A Chemical Interpretation of Life Processes.

In the consideration of the chemical changes which take place in nature, a classification which has been suggested in the past and for which there is considerable justification, divides reactions into two groups: those occurring in living matter, and those occurring in non-living matter. It is evident that many of the chemical reactions which occur in living matter may be caused to take place by artificial means in non-living matter. At the same time, the changes in living matter, during the time that such matter, by common consent, is said to be living, possess characteristics which, when considered from certain points of view, appear to set off such changes from those occurring in non-living matter. In this chapter, an attempt will be made first to present the chemical phenomena of living matter from a strictly chemical point of view, to show the analogies between the two groups of reactions, interpreting both on the basis of the same fundamental laws of chemistry, and finally to present from this chemical viewpoint certain developments of the phenomena of life processes in connection with related branches of science.

In order to develop these views in a systematic way, it will be necessary to refer to and to repeat some of the classifications and theories which were presented in the earlier chapters of this book as well as in other connections. The topics under discussion involve chemical change. The development of a general theory of chemical reactions which would include reactions both of inorganic chemistry as well as of organic chemistry is a necessary forerunner of the further views. A theory of this sort is the "Addition Theory of Chemical Reactions" which was presented in a somewhat extended form elsewhere.[1] According to this theory, an addition compound is the first product formed

[1] "Chemical Reactions; Their Theory and Mechanism."

when two or more molecules react. This addition compound may then decompose or react farther in a number of different ways, the conditions, such as the relative concentrations of the reacting constituents, removal of products, etc., determining in any one case the actual products obtained. If a reaction does not attain equilibrium and two or more decomposition reactions are possible for the addition compound, other things being equal, the reaction taking place with the greatest velocity will be the one observed experimentally. With a monomolecular reaction, the velocity is directly dependent in some way on the internal electronic structure of the reacting molecule. Some of the more recent theories which have attempted explanations of the phenomena of monomolecular reactions were presented in Chapter IV. At the same time, the decomposition of the intermediate addition compound in the reactions of higher orders is fundamentally in every case a monomolecular reaction and dependent undoubtedly upon the electronic configuration within the molecule. Reaction in any case involves rearrangement of the electrons, their distributions and motions, accompanied by separation of atoms and simpler molecules. With more complex addition compounds, greater numbers of modes of decomposition would be possible. A number of such reactions illustrating the possibilities of the addition theory have been presented in different connections.

The second step in the development includes the introduction of catalysts into the treatment of chemical reactions. From the considerations presented in the earlier chapters it will have been made evident that no generally satisfactory classification or theory of catalytic actions as distinct from other reactions exists, but that whatever definition or description is used, the ordinary laws and relations of chemistry are applicable. (It is well to repeat this fact frequently because of the confusion created by some authors in writing of catalytic reactions.) The phenomena of catalysis may make themselves evident experimentally according to any of the definitions or classifications proposed, by a change in the velocity of a given chemical reaction upon the addition of the catalyst, or where two or more reactions are possible, by one being favored over the other in the sense that the addition of the catalyst results in the products of one

of the possible reactions being increased more than the products of the other reactions. For the sake of completeness, it may be mentioned that a catalyst may be involved in a reaction without causing these effects according to certain views, and also that radiations of various frequencies might be included under the term catalysts. The theory of catalytic actions which appears to the writer to cover the facts most satisfactorily is that which considers that in a catalytic reaction the chemical composition of one of the initial and final products is the same. The reaction may take place in two or more steps. The change in velocity is only one of the signs to show that a reaction is catalytic. A change in the proportions of reaction products is another. These relations have been developed in several places in this book as well as elsewhere.

The next step involves the consideration of enzymes as catalysts. Enzymes are catalysts produced by living matter, which, even in the absence of the life process, are able to exert catalytic actions on more or less definite chemical reactions. The velocities of these reactions are changed, or the products may be obtained in different proportions in the absence and in the presence of the enzyme preparations. These enzymes appear to possess certain characteristics which are generally associated with living matter. They are inactivated under conditions which destroy life, such as heat, addition of certain substances which may be said to act as poisons, etc. Such behavior is not, however, limited to enzymes or catalysts produced by living matter. The striking investigations of G. Bredig [1] and his co-workers on "Inorganic Ferments" must be spoken of in this connection. Colloidal solutions of metals such as platinum, gold, silver, etc., prepared by passing an electric arc between two electrodes of the metal under water, increase the rate of decomposition of hydrogen peroxide solutions. The enzyme catalase exerts a similar action. The activities of both the inorganic ferment and the enzyme were increased by increase in temperature up to a certain optimum and then were decreased, each ferment having its own optimum temperature. Small quantities of certain sub-

[1] G. Bredig and R. Müller von Berneck, *Z. physik. Chem. 31*, 258 (1899); G. Bredig and K. Ikeda, *Z. physik. Chem. 37*, 1 (1901); G. Bredig and W. Reinders, *Z. physik. Chem. 37*, 323 (1901); G. Bredig, *Ergebnisse der Physiologie 1*, 134 (1902); G. Bredig and M. Fortner, *Ber. 37*, 798 (1904).

stances such as hydrogen cyanide, hydrogen sulfide, mercuric chloride, etc., inhibited the actions of the inorganic ferments and were therefore called poisons. Other substances such as formic acid, hydrazine, etc., increased the activities. The analogies between the actions of the inorganic ferments and some of the actions of certain enzymes are striking, but must not be pushed too far at present. While the chemical compositions and structures of most of the enzymes are practically unknown, the compositions of metallic colloidal solutions are not known to any satisfactory extent either, since small amounts of "foreign" substances may exert considerable influence on their stability and behavior aside from their catalytic actions.[1]

Before proceeding to the next step in the developments, a few words may be said relative to "hormones" and so-called "vitamins" or perhaps better "food hormones." The study of the actions included under these terms has been carried on extensively in the past ten years, and the literature, especially of the latter subject, is almost overwhelming. These actions have frequently been compared to enzyme actions. Just how far the comparison is justified cannot profitably be entered into in the present connection. Enzyme actions can be studied with definite chemical reactions outside the living organism and can consequently be made to yield comparable quantitative data upon which to base conclusions. Such chemical reactions have not as yet been found for studying hormones and vitamins, and all the results available at present for these have been obtained by means of studies *in vivo*. All of these actions, including enzyme, hormone and vitamin, may be considered to be catalytic. All of them retain certain properties which are derived directly from the life processes of which they form, if not the most important feature chemically, at least an important part. These properties include the temperature conditions for optimum action, conditions for inactivation, etc. These similarities are not, however, sufficient reason for placing the actions of hormones and vitamins in the same class as enzymes until more is known of their behavior. In view of the lack of definite chemical knowledge concerning them and their actions, they will not

[1] Cf. H. T. Beans and H. E. Eastlack, *Jour. Amer. Chem. Soc.* **37**, 2667 (1915).

be considered farther here. Attention is directed to them since they form a group of catalysts in living matter which parallel the enzymes, and which may ultimately be classed with them, both as separate groups of a larger division comprising reactions taking place in life processes.

To return to enzyme actions in life processes, the chemical equations (4) which were given in the last chapter as representing some of the possible changes may be repeated as follows:

$$\left[\begin{array}{l}\text{Enzyme} \\ \text{Substrate} \\ \text{(or Products)} \\ \text{Water}\end{array}\right] \begin{array}{ll} = \text{Enz.} + \text{Substr.} + \text{Water} & \text{(a)} \\ = \text{Enz.} + \text{Products} + \text{Water} & \text{(b)} \\ = \text{(Enz. Products)} + \text{Water} & \text{(c)} \\ = \text{(Enz. Substr.)} + \text{Water} & \text{(d)} \end{array} \quad (1)$$

It will be recalled that with a complex protein, for example, a number of equations (symbolized by equation (b)) representing different sets of products would be possible, the reactions observed or predominating depending upon the special enzyme and substrate preparations, and upon the relative velocities of the reactions and the conditions under which these are proceeding.

The most striking feature of the chemical changes occurring in living matter, and in fact of life processes themselves, is their continuity. As long as life continues definite chemical changes occur. The same or similar substances are transformed chemically to produce the definite chemical substances which are essential to the life process of the given species. As outlined in the preceding chapter, the presence of specific enzymes causes the reactions to follow the required course and to yield the products essential for the life process. In order to have the life process continuous, the formation of enzymes in the chemical reactions is necessary. That is to say, an enzyme causes certain reaction products to predominate in a complex chemical reaction. Under the conditions of most of such reactions, certain other products will be eliminated or discarded, at the same time that the original enzyme substance may be inactivated or destroyed. Fresh enzyme must therefore make its appearance, and this must necessarily arise from the products of the reactions which had previously taken place. This would signify according to equations (1) that the enzyme involved in the reaction would be inacti-

vated or destroyed by further chemical action, but that the substances symbolyzed by "Products" would either contain newly formed enzyme or contain material which on further reaction would be transformed into enzyme. These enzyme reactions may also proceed in a way to produce complex bodies from simple substances, the substrate being the latter, the products the former. Enzymes show these synthesizing actions as well as the decomposing actions. Because of the experimental conditions generally employed in studying enzyme actions *in vitro*, the experimental results obtained refer mainly to the decomposing actions, but it is evident that in the living animal or plant the synthetic actions of enzymes are of equal importance.

The formation of fresh enzyme material as part of the products of an enzyme action furnishes a special case of catalytic acceleration described in Chapter II. If old enzyme is inactivated or destroyed as rapidly as fresh enzyme is produced, a steady state is reached. If fresh enzyme is produced more rapidly than old enzyme is destroyed, a state of increased change or growth, either normal or pathologic, may result.

Attention is focussed here on the actions of the enzymes in living matter. The higher forms of living matter are of great complexity when considered from such a chemical point of view. The existence of this complexity must be recognized but at the same time will not be entered into directly in connection with the interpretation of the changes on the basis of the enzyme actions. Thus it will not be practicable to enter into such questions as the influence which may be exerted by the form of the living matter involving such relations as the possibility of forming an enzyme in one part of the organism and exerting its action in another part, etc. The discussion will be limited to the possibility of a chemical interpretation of the relations and of the chemical mechanism which may be involved.

Outside directive agencies of chemical character apparently are not required to produce the special enzymes needed to bring about the chemical reactions necessary for the continuation of life processes. Life processes in chemical terms may therefore be said to consist of self-perpetuating cycles of definite chemical reactions producing, among other products, enzymes which favor the definite chemical reactions, etc. Any one cycle will continue

as long as the suitable substances (substrates) are provided and the external conditions remain unchanged or favorable. If a change occurs in the sense that a different substrate is added, the products not removed as before, foreign substances which themselves are not changed by the enzyme action added, or external conditions such as temperature, etc., changed, then the enzyme which exerted its action before may be entirely inactive or still be active but may cause different products to be formed. In the first case the life process ceases. In the second case, with different products the fresh enzyme produced may also be different and then itself produce different changes in the substrate upon which it, in turn, acts. The nature of the substrate provided, the external conditions which may be grouped under the term environment, and the enzyme acting and produced, will determine the actual life process occurring. With small and temporary variations in substrate and external conditions, the enzyme actions and enzyme produced would not be expected to depart much from the original enzyme and its actions, and will return to these when the former conditions are restored. With small changes in substrate or in external conditions, a change in enzyme and enzyme actions may occur, and if the former changes are continuous within limits, the latter actions would be modified continuously but not destroyed. This behavior may perhaps be a chemical interpretation of growth in living matter. Here again the great complexity of many forms of living matter may make it difficult to accept such a comparatively simple viewpoint or explanation for the many interrelated and mutually dependent chemical changes which are taking place. It can only be said that if a chemical interpretation is attempted, and fundamentally the changes involved are chemical in character, a start must be made somewhere, and enzyme actions at the present time offer the most promise. Simple explanations of apparently complex phenomena may not be correct, but at any rate they give a working basis, and may be used until better explanations are available.

The changes in substrate, environment, and enzyme character which have been spoken of may be considered somewhat farther since they lead to interesting conclusions. The orderly continu-

ous change which is known as growth represents one set of possible phenomena. Similar changes not accompanied by growth may also occur. The changes in substrate and in enzyme are reciprocal—they mutually influence each other when they occur. The changes in enzymes and in enzyme actions cannot be controlled directly, but the changes in substrate and in environment permit of a certain amount of control. This will be illustrated presently in considering some of the experimental evidence relating to these phenomena. If the changes in substrate or in environment or in both are small and continuous, and change in enzyme and enzyme action occurs, then the phenomenon would be considered as adaptation to the environment. The continuous modification of substrate or of environment or of both would then result in a different, or a modified, chemical reaction, this in turn in a different enzyme and enzyme action, the modifications increasing progressively until the new cycle conforms to the new conditions imposed from without. If several different cycles of changes could occur under the new conditions, then it might be expected that they would show different degrees of adaptability, and only certain of the cycles adapt themselves. This might be considered to be the chemical significance of the term "survival of the fittest." Further, these changes when occurring in the complex structures of highly organized living matter of plants and animals may result in modifying their forms and reactions.[1] Such changes might be considered as developments of the forms of living matter. Fundamentally, they are changes, but they may also be called developments. In the past fifty years the word evolution has supplanted the vaguer term development, so that the views here outlined might be considered to represent a chemical interpretation of the mechanism of evolution.

In this connection attention may be called to the fact that while the cell is the biological unit of living matter, enzymes may be considered chemically to form the distinctive characteristics of living matter since they are the directive agencies controlling the course of the chemical changes. The composition of living matter is fixed by the combinations of atoms of elements in certain ways to form molecules; the characteristic structures of

[1] Cf. E. S. Goodrich, *Science* 54, 529 (1921); "Some Problems in Evolution."

living matter are determined by cells and micelles.[1] From the chemical point of view as outlined, enzymes are the controlling factors of life processes, and distinguish the chemical reactions of such processes from those of inanimate nature because of the self-perpetuating cycles of changes which they control.

In speaking of enzymes and their actions in this way, the conditions under which enzymes can act must be kept in mind. Cells have been termed the biological units of living matter, but except under suitable conditions, cells do not show the distinguishing feature of living matter in contrast to non-living matter, that is, the ability to reproduce or the continuity of the changes. Similarly, enzymes manifest their actions as directive agents under suitable conditions. Certain of the properties and actions of enzyme preparations may be studied by means of simple laboratory experiments, but the conditions under which they might be expected to show the phenomena associated with life processes have not as yet been realized experimentally apart from the living organism. These conditions include such factors as supply of proper substrates in the necessary concentrations, removal of part of the products of the reactions, absence of interfering substances, etc. Some of these factors will be considered somewhat farther in the following chapter on "Contact Catalysis" in connection with the part played by membranes with reactions involving substances present in several phases. This side of the problem will be ignored in the present connection, but with no intention of minimizing its importance.

The study of life processes from a chemical point of view has been pursued by J. Loeb for a considerable number of years. The following quotations from some of his writings are of interest especially in connection with the problems considered in the preceding pages.

"We know that growth and development in animals and plants are determined by definite although complicated series of catenary chemical reactions, which result in the synthesis of a definite compound or group of compounds, namely, nucleins.

"The nucleins have the peculiarity of acting as ferments or enzymes for their own synthesis. Thus a given type of nucleus will continue to synthesize other nuclein of its own kind. This determines the continuity of a

[1] The word "micelle" may be taken to signify the unit of colloidal protein or other material in a complex molecule or particle. It represents a more or less definite unit of matter, not as rigidly definable at present as the molecule, but useful in considering colloids and their behaviors.

species; since each species has, probably, its own specific nuclein or nuclear material. But it also shows us that whoever claims to have succeeded in making living matter from inanimate will have to prove that he has succeeded in producing nuclear material which acts as a ferment for its own synthesis and thus reproduces itself. Nobody has thus far succeeded in this, although nothing warrants us in taking it for granted that this task is beyond the power of science.[1]"

"The essential difference between living and non-living matter consists then in this: the living cell synthetizes its own complicated specific material from indifferent or non-specific simple compounds of the surrounding medium, while the crystal simply adds the molecules found in its supersaturated solution. This synthetic power of transforming small "building stones" into the complicated compounds specific for each organism is the "secret of life" or rather one of the secrets of life.

"What clew have we in regard to the nature of this synthetic power? We know that the comparatively great velocity of chemical reactions in a living organism is due to the presence of enzymes (ferments) or to catalytic agencies in general. Some of these catalytic agencies are specific in the sense that a given catalyzer can accelerate the reaction of only one step in a complicated chemical reaction. While these enzymes are formed by the action of the body, they can be separated from the body without losing their catalytic efficiency.[2]

"The constant synthesis then of specific material from simple compounds of a non-specific character is the chief feature by which living matter differs from non-living matter."[3]

Some of the quantitative data published by Loeb in recent years bearing upon the changes occurring in life processes will be presented. The study[4] of the effect of temperature on the duration of life of the fruit fly (*Drosophila*) freed from all microorganisms and with an adequate food supply gave a temperature coefficient of between two and three for a 10° rise in temperature, a value of the same order of magnitude as the temperature coefficient of a chemical reaction. The ratio of the duration of life of the insect to the duration of the larval stage, and the ratio of the larval to the pupa stage, were found to be approximately constant for all temperatures studied. It was suggested that the duration of life was determined by the production of a substance leading to old age and natural death or by the destruction of a substance or substances which normally prevent old age and natural death.

The quantitative study of regeneration in the stem of

[1] J. Loeb, "The Mechanistic Conception of Life." University of Chicago Press, Chicago, 1912. P. 227.
[2] J. Loeb, "The Organism as a Whole From a Physicochemical Viewpoint," G. P. Putnam's Sons, New York and London, 1916. P. 23.
[3] J. Loeb, "The Organism as a Whole From a Physicochemical Viewpoint," P. 29.
[4] J. Loeb and J. H. Northrop, *Proc. Nat. Acad. Sci.* 3, 382 (1917); *J. Biol. Chem.* 32, 103 (1917).

Bryophyllum calycinum gave the following results.[1] Equal masses of sister leaves produced equal masses of shoots and roots in equal times and under the same conditions, regardless of the number of shoots produced. The mass of shoots and roots produced by different masses of sister leaves in equal times and under equal conditions was approximately in direct proportion to the masses of the leaves. When a piece of stem inhibited the production of shoots and roots in a leaf of *Bryophyllum* connected with it, the stem gained in mass an amount approximately equal to the mass of shoots and roots the leaf would have produced if it had been detached from the stem. The inhibitory influence of the stem upon the formation of roots and shoots in the leaf apparently was due to the fact that the material available and required for this process flowed into the stem. In other words, the principle of chemical mass action was found to apply to the problem of growth in the given case.

The phenomena which have been included under the terms "Forced Movements" and "Tropisms" whose scientific importance and significance were developed mainly by J. Loeb may also be spoken of in this connection.[2] The tropisms which have been studied include galvanotropism, heliotropism, geotropism, stereotropism, chemotropism, and thermotropism. Explanations for the actions observed under the influence of the various forms of energy were based upon the chemical properties of the substances affected and possible changes in the active masses of the substances under the different conditions, and satisfactory conclusions reached. It is possible that enzyme actions also are involved, perhaps after or at the same time as the direct chemical effects which were observed, and that the reciprocal actions of the changes in substances and the enzyme actions are responsible for the changes observed.

In all of the work described, the changes are shown to follow the chemical mass action principle. The question still remains open, however, whether it is the concentration or mass of the reacting constituent which is transformed which is increased, or whether it is the concentration or the nature of the enzyme which

[1] J. Loeb, *J. Gen. Physiol. 1*, 81 (1918); *2*, 297, 651 (1920); *Science 54*, 521 (1921).

[2] Cf. J. Loeb; "Forced Movements, Tropisms and Animal Conduct." Monographs on Experimental Biology. J. B. Lippincott Company, Philadelphia and London, 1918. J. Loeb and J. H. Northrop, *Proc. Nat. Acad. Sci. 3*, 539 (1917).

is changed. The data available at present do not permit of a decision on this point being reached.

Some of the further experimental studies which bear upon the problems discussed in the earlier pages of this chapter will now be taken up. One of the main questions involved includes the development or production of enzymes in and by living organisms and the effect on these enzymes of changes in the medium or environment. During the growth of higher plants and animals the characters of the enzymes frequently change as the organisms develop. These changes are fundamentally of the nature of the changes under discussion. The conditions under which these changes occur do not, however, permit of ready alteration experimentally of the external conditions or environment. The possible changes in enzyme actions resulting are of great interest, but because of lack of experimental control in most cases are not as satisfactory for a discussion of this sort. They will not, therefore, be spoken of farther in this connection. More satisfactory studies of the desired nature have, however, been begun with some of the lower organisms such as yeasts and bacteria. By suitable changes in the nutrient media, the amounts of certain enzymes have been increased to a considerable extent. Reference may be made in this connection especially to the studies of Euler and his co-workers.[1] It was found that yeast (definite strains from beer fermentations) showed a maximum growth as well as a maximum formation of sucrase at pH 5-6. In general, conditions which favored the former favored the latter as well, although this was only a rough parallelism. However, a more recent study [2] showed that the growth stimulant probably was not the same substance which increased the rate of sucrase formation. A partial separation of the two substances was effected by extraction of the former with benzene, by adsorption with fuller's earth, and by precipitation with phosphotungstic acid.

An extended investigation of the formation of urease by bacteria was published by M. Jacoby.[3] He followed the change in amounts of urease produced in urease forming bacteria by the

[1] For a summary of this work as well as for references to the original literature cf. H. Euler, "Chemie der Enzyme, 1. Teil. Allgemeine Chemie der Enzyme," 1920. Pp. 291-6.
[2] E. W. Miller, *J. Biol. Chem.* *48*, 329 (1921).
[3] M. Jacoby, *Biochem. Z.* *79*, 35 (1917).

addition of a number of organic substances to the nutrient mixture. A number of these substances, including hexoses and three carbon sugars, increased the amounts of urease considerably, while a larger number, including various carbohydrates, had no apparent effect. It was also found by Euler and Asarnoj that the addition of starch to the nutrient solution increased the production of amylase by Aspergillus niger.[1]

The increases in enzyme concentrations described, and others which might be quoted, brought about by suitable alterations of the media, are of importance, but the changes which have been called "acclimatization" appear to be of greater interest and significance.

The ability of a yeast to ferment a given sugar depends to a certain extent upon its previous history. Thus, it has been possible to increase the galactose fermenting action of a yeast to a considerable extent. One of the methods of doing this may be outlined briefly as follows: Two grams of washed and pressed yeast were mixed with 200 cubic centimeters sterilized nutrient solution containing the ordinary salts together with 4 grams asparagine and 20 grams of the carbohydrate in question, and allowed to stand at ordinary temperatures for different lengths of time. The solution was then decanted from the yeast, the latter washed, and dried on clay. The fermenting actions on different carbohydrates, calculated to the common basis of dried yeast, were determined by measurement of the carbon dioxide evolved in a definite period of time. One series of experiments in which a top yeast was acclimatized to galactose, gave for the original fermenting action a ratio of 1:50 for the actions on galactose and on sucrose, while after treatment with galactose, the ratio was found to be 1:6.5. An eight fold increase in fermenting action on galactose had been obtained.[2] With bottom yeast, the final ratio 1:2.4 was obtained. The juice obtained from acclimatized yeast was also found to ferment galactose.[3] The question of acclimatization is treated at some length by A. Harden in his monograph on "Alcoholic Fermentation."[4]

[1] H. Euler and S. Asarnoj, *Fermentforschung 3*, 318 (1920). The sucrase activity of Aspergillus niger was found to be increased about 30% by the addition of peptone.

[2] H. Euler, I. Laurin, and A. Pettersson, *Biochem. Z. 114*, 277 (1921).

[3] A. Harden and R. V. Norris, *Proc. Roy. Soc. London (B) 82*, 645 (1910).

[4] Pp. 109-112.

These results show in every case an increased action by an enzyme which, however, was present before the treatment even if only to a very small extent. In principle, such an increase is of as great significance as the formation of an entirely new enzyme not present before, but even so, it is of interest to note that this problem of enzyme formation also appears to have been solved. "The question, if, and under what conditions it would be possible, by chemical or physical influences on the cell to produce enzymes which otherwise are foreign to the given microörganisms, is still open; it is difficult to answer directly, as it is always possible that a trace of the corresponding enzyme might be present, so that a new formation did not occur. The writer (Euler), starting with the view that a marked and reproducible influence could be obtained by symbiosis, sought for and found the formation of amylase in microörganisms, in which previously by the same methods, no indication of the presence of this enzyme could be obtained." [1]

The changes in bacterial cultures which may be brought about by changes in the media in which they grow may properly be included here. The question of growth in purely synthetic media is also involved. Careful studies, qualitative and quantitative, of the actions of enzymes obtained from bacteria grown under various conditions are not common. It may be of greater interest to present in this connection extracts from an address [2] by a leading worker in this field as representing the present status of the problem.

"The diphtheria bacillus, grown in appropriate nitrogenous media containing no utilizable sugar or an amount of sugar which the organism can use up without inhibiting its further activity, will produce a very potent soluble toxin. If the *same* organism is grown in the *same* nitrogenous medium, to which is added sufficient utilizable sugar so that the organism cannot use it up, it will be found that no toxin whatever will appear in the culture. Similarly, the colon bacillus grown in sugar-free nitrogenous media will produce indol, ammonia, hydrogen sulphide and other products indicative of the break-down of protein; but the *same* organism grown in the *same* nitrogenous medium, to which utilizable sugars are added, will not contain any of these products indicative of protein break-down. On the contrary, the characteristic products are organic acids, carbon dioxide and hydrogen.

"The proteus bacillus is one of a considerable number of bacteria which produce a soluble enzyme in sugar-free gelatin, which liquefies this protein. The sterile filtrate of such a liquefied gelatin culture will contain enough

[1] H. Euler, "Allgemeine Chemie der Enzyme," p. 296.

[2] "Recent Developments in Intestinal Bacteriology," by A. I. Kendall. Published in *Am. J. Med. Sci. 156*, 157 (1918).

free enzyme to liquefy an additional amount of gelatin. The addition of a *small* amount of utilizable sugar to gelatin cultures of the proteus bacillus will prevent temporarily the formation of this enzyme in an active state and the addition of a *considerable* amount will *permanently* prevent the development of the gelatin-liquefying enzyme. It is worthy of note that the mature, soluble, gelatin-liquefying enzyme, freed from bacteria by filtration through a porcelain filter, will liquefy sterile gelatin containing the same sugar which *in culture* prevented the formation of the enzyme, clearly suggesting that the presence of utilizable carbohydrate prevented the *elaboration* of the enzyme, but had no effect upon the *action* of the enzyme once it was excreted in an active state.

"The relation between the factors which form the production of this proteolytic enzyme and those which are associated with its action when it is mature is even more striking. Chemical examination of cultures (free from utilizable carbohydrate) in which the enzyme develops in increasing proportions shows the presence of increasing amounts of ammonia. A similar examination of sterile gelatin mixtures (with or without carbohydrate), in which the germ-free enzyme induces liquefaction, fails to reveal any increase whatsoever in ammonia. Apparently the activity of the enzyme is independent of ammonia formation. Nevertheless, ammonia formation invariably occurs when the enzyme is formed by the bacillus. The facts presented would seem to justify the following deductions: The soluble gelatin-liquefying enzyme of Bacillus proteus is formed when the organism utilizes protein for its energy. It is not formed in an active state when utilizable carbohydrates are continually available for energy. (Small amounts of carbohydrate insufficient to prevent the development of the organism have been shown in similar experiments to inhibit enzyme formation until the carbohydrate is used up. Acid within the limits of tolerance of the organism does not inhibit enzyme formation.) The function of the enzyme is to prepare protein for assimilation by the organism, as the enzymes of the alimentary canal of man prepare proteins for assimilation. Ammonia formation is a measure of the deaminization of the assimilated protein fragment and not a concomitant feature of the action of the enzyme *per se*. The ammonia is 'bacterial urea.' Other organisms which form similar soluble proteolytic enzymes react in like manner to the presence of utilizable carbohydrates.

"The protective or sparing action which utilizable carbohydrate exhibits for protein or protein derivatives in cultures of bacteria has its counterpart in higher organisms. The underlying principle is apparently analogous to that in man: Physiologists have long stated that the oxidation of carbohydrates protects the protein of the body. Carbohydrates, in other words, are protein sparers, and, as Howell has aptly stated it, 'as the carbohydrate food is increased the protein food may be diminished down to a certain irreducible minimum, which is probably the amount necessary for the reconstruction of new tissue.'

. . . . . .

"The sparing action of utilizable carbohydrate for protein in cultures of bacteria has a deeper significance than has been realized hitherto. The diphtheria, colon and proteus bacillus, to mention merely those referred to above, form widely different products as the result of their growth in nitrogenous media from which utilizable carbohydrates are excluded. The same is equally true for typhoid, paratyphoid, dysentery, hemorrhagic septicemic, tetanus, "gas," symptomatic anthrax and many other pathogenic bacilli, cholera and other vibrios and a large number of saprophytic organisms as well. Stated differently, it is positively known that diphtheria and tetanus bacilli form highly specific soluble toxins as they develop in protein media. They form innocuous fermentation products, chiefly acids, as lactic and acetic, from the same media to which utilizable carbohydrates

are added. That which makes diphtheria and tetanus bacilli formidable, in other words, is apparently inseparably associated with their growth in nitrogenous but carbohydrate-free media. The antithesis of this specificity of products developed in nitrogenous, sugar-free media is manifested in the remarkable similarity of products formed in the same media which contain utilizable carbohydrate in addition. The nitrogenous products formed by typhoid, dysentery, cholera and other pathogenic organisms are unknown as yet, but the simple addition of utilizable carbohydrate to cultural media in which they are grown causes them to produce fermentation products, as lactic acid, precisely as the diphtheria bacillus does under similar circumstances. The chemical products formed by these bacteria in the presence of utilizable carbohydrate are potentially those produced by the Bulgarian bacillus; that is to say, a large number of bacteria pathogenic for man become potentially lactic acid bacilli when they are grown in fermentation media, and from this point of view, therefore, their specificity of action is inseparably associated with the utilization of protein for energy.

"Typhoid, dysentery, and diphtheria bacilli do not ferment lactose. If milk contained dextrose in place of lactose, or if at least 0.5 per cent of dextrose were added to it, these organisms would produce sour milk as the result of their growth in it and this sour milk would not differ qualitatively from that produced by the Bulgarian bacillus. Furthermore, so long as the bacteria were confronted with this dextrose they would continue to make sour milk until the acidity reached a degree incompatible with their further growth. If the utilizable carbohydrate were removed, of course they would act once more upon the protein."

In speaking of intestinal bacteria, Kendall stated:

"There appears to be an intimate relationship between the character of the diet and the nature of the intestinal flora. This relationship, bacterially considered, is manifested by an adaptive intestinal acclimatization of fairly definite types of bacteria. Changes in the diet, if prolonged, tend to change the types of bacteria. A change in the products of metabolism of intestinal bacteria is also induced, depending upon the presence or absence of carbohydrate. . . . Bacteria which are normally acclimatized do not produce metabolic products widely at variance with the well-being of the host. . . . Bacterial acclimatization and adaptation is the resultant of complex reciprocal activities between host and parasite."

It will hardly be necessary to enter farther into this question in the present connection. Changes in bacteria brought about by differences in nutrient media are clearly recognized. These changes have been shown experimentally to be accompanied by changes in enzyme actions in some cases. Undoubtedly, further study will show the connection with enzymes and their actions in all cases of change in bacterial nature. It should be possible with the means at hand and the data already available to carry out conclusive studies of this kind. In fact, bacterial enzymes, obtained from bacterial cultures after using various media, offer an extremely fertile field for the study of the relations between the formation and properties of enzymes and the chemical and biological mechanism of life processes.

The views here developed are based upon the following successive generalizations: (a) General (addition theory) of chemical reactions; (b) Catalytic reactions as a group of chemical reactions; (c) Enzyme reactions as a group of catalytic reactions; (d) Life processes interpreted as controlled essentially by enzymes. The application of these views might obviously be carried over to other branches of science, explanations developed based upon these fundamental conceptions, and evidence brought forward to support the explanations.

One more feature of the problem of living matter may be mentioned. The production of enzymes and their actions were considered to be the essence of living matter. Enzyme actions have been shown to be chemical reactions fundamentally. Enzyme production then forms the chemical counterpart of the production of life. Reasoning from the basis of the chemical views which have been presented, it may be said that either the life process is created or begun continuously in and to form living matter, every new formation of enzyme representing such a creation or beginning, or it is not created at all, the production of new enzyme material being a part of the chemical change or part of the products formed by the action of the old enzyme on the available material. Going back one step farther, according to the latter hypothesis, a separate causation of life need not be sought. Life originally would then have been the chance result of certain catalytic actions (later to be known as enzyme actions) on suitable material, which formed continuously new catalytic (or enzyme) substances (auto-catalytic in the present terminology), resulting in the cycles of changes described in this chapter. The two possibilities present themselves in a comparatively simple manner; either the continuous ever-present creation of life as long as living matter exists or has existed, in place of the one creation (or possibly several creations) at some remote period in the past, or no creation in the extra-scientific sense at any time, but a continuous cycle of changes which can be interpreted on the basis of definite well-known chemical principles, in which the continuity, change, development, evolution, and even the beginning, require no new fundamental concepts of science or philosophy.

Chapter VIII.

Contact Catalysis.

The term "contact catalysis" has been used at various times to include catalytic reactions in which the substances involved occur in two or more phases. In order to discuss such reactions with as much understanding as possible, it is well to consider the significance of the definitions, the limitations of the phenomena, and their relations to other chemical and physical changes, before speaking of a number of individual reactions.

"Contact" reactions or processes are stated as a rule to include chemical reactions which take place in heterogeneous systems. In the present connection, in the consideration of reactions taking place in heterogeneous systems, it will be postulated that the substances taking part in the reaction must be present in two or more phases before the chemical change has occurred. Each substance need not be present in two phases, but substances existing initially in at least two phases must react. They may be present in one, two, or any number of phases after the reaction has occurred, but this is of no direct importance in the classification of the reactions. This view at once excludes reactions in which gases are evolved or precipitates formed in changes taking place in solutions initially homogeneous, etc., and, in fact, all reactions in which the substances are originally present in one phase or as a homogeneous system. Also, for the present, reactions in which radiations of various types are known to play a prominent part will be excluded. This appears to be advisable as the relations of such reactions to those in which radiation influences are not so apparent are not as yet well developed. In view of the extensive experimental work which is in progress along these lines, it may confidently be expected that, in the near future, relations will have been developed to permit of satisfactory classification of radiation reac-

tions. At the same time, an increased knowledge and better understanding of all chemical reactions is bound to result from the study of phenomena as fundamental for chemical change as radiation.

The reactions which take place in heterogeneous systems in which the substances are present initially in two or more phases are, therefore, to be termed "contact reactions." The reactions which may be included under the term "contact catalysis" bear to contact reactions exactly the same relations which catalytic reactions in general bear to chemical reactions in general. Whatever definition is assumed to apply to one set of relations may be carried over to the other set of relations. It was pointed out in the earlier chapters of this book that the writer prefers to consider a catalytic reaction as a reaction in which the chemical composition of one of the final products of the reaction is the same as that of one of the initial substances. This definition is evidently directly applicable to contact catalytic reactions. The fact that a catalytic substance has taken part in the contact reaction may be made apparent as with other reactions by a change in the velocity of the reaction, or by a change (complete or partial) in the products obtained. The use of a different definition of catalytic action, however, will not affect the view of the relations outlined here between contact catalytic reactions, contact reactions in general, and chemical reactions as a whole. This classification will hold without modification for any chemical theory of catalysis which has been suggested, but if the term catalysis is to be retained in chemical literature, the writer prefers the definition first given.

Since, in heterogeneous systems, reactions between substances present in different phases take place at or near the surfaces of the phases, a review of some of the recent work bearing upon the condition and behavior of substances at interfaces will be given. It is only very recently that light has been thrown on the chemical states of substances under such conditions. Before the studies which will be spoken of were made, it was necessary to take refuge in general statements based upon inconclusive experimental material in describing the conditions and the actions at such interfaces.

The phenomena which are included in the term "adsorption"

must be taken up in connection with the relations to be described. Adsorption may be defined as the difference in the composition of the surface layer at the contact of two phases and the compositions in the main bodies of these phases.

The recent advances in the knowledge of the conditions of surfaces, of reactions taking place at interfaces, and of adsorption, are due in the main to the work of I. Langmuir and of W. D. Harkins.

The striking feature of the advance made by Langmuir [1] in the treatment of the conditions at interfaces is the emphasis which he placed upon the chemical nature of the forces involved in adsorption, surface tension, evaporation, crystallization, etc., these forces being considered not to differ "in any essential respect from the forces which cause the formation of typical chemical compounds." [2] These same forces are active in solids and liquids which are considered in any given case to consist of one large molecule, the atoms of which are held together by chemical forces. Langmuir is definite with regard to the fact that these chemical forces which cause the various phenomena are essentially the same. At the same time, a point must be mentioned which will be taken up again later in this chapter. In attempting to define these chemical forces in explicit terms, Langmuir did not present as satisfactory a picture. In various places he spoke of chemical forces acting by means of "primary" valences and "secondary" valences. He gave the characteristics of these forces in discussing the interatomic and intermolecular forces involved in the structure of matter,[3] but to the writer there appears to be no essential difference between these two forms of valence as defined, although it must be added that the use he made of the two conceptions indicated definite differences, as will be pointed out later. This is, however, a minor factor in these considerations. Langmuir made clear the fact that the forces are chemical and not physical in nature, and this is the main consideration in the present discussion.

The first point of interest in Langmuir's treatment relates to the question of the nature of the surfaces of solids and liquids

[1] I. Langmuir, *Met. Chem. Eng.* *15*, 469 (1916); *Jour. Amer. Chem. Soc.* *38*, 2221 (1916); *39*, 1848 (1917); *40*, 1361 (1918); *Chem. News* *123*, 225, 237 (1921).

[2] *Jour. Amer. Chem. Soc.* *39*, 1901 (1917).

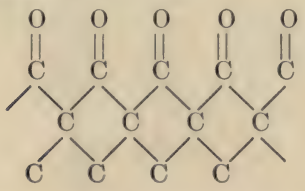
[3] *Jour. Amer. Chem. Soc.* *39*, 1853 (1917).

in contact with gases. It was pointed out that there is not a transition layer either for solids or liquids "in which the density varies by continuous gradations from that of the solid to that of the surrounding gas or vapor." [1] The transition was considered to be abrupt, and for solids to be accompanied by a greater density of the packing of the atoms in the surface layer than in the body of the solid. Following the views of the arrangements of atoms in crystals developed by means of x-ray studies, it was shown that "the surface must be looked upon as a sort of checkerboard containing a definite number of atoms, of definite kinds, arranged in a *plane* lattice formation. The space between and immediately above (away from the interior) these atoms is surrounded by a field of electromagnetic force more intense than that between the atoms inside the crystals." [2] "The only essential differences between liquids and solids seem to lie in the mobility of liquids and in those properties which are directly dependent on mobility. As a result of this mobility, the definite lattice arrangement of the atoms of solids gives way to the irregular arrangements characteristic of liquids." [3] The atoms are all assumed to be combined as one large molecule in a liquid, the mobility being due to some sort of tautomerism. It is obviously impracticable to enter in detail into the evidence which was presented by Langmuir in connection with these deductions.

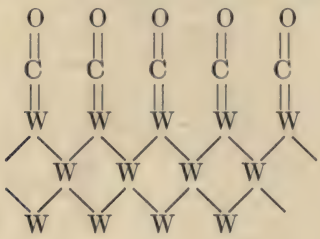
The actions of the solid and liquid surfaces in combining with substances present initially in other phases (so-called adsorption) was treated by Langmuir from the point of view just outlined. The forces acting are chemical in character, and, because of the stronger electromagnetic fields existing at surfaces, are perhaps more intense than under different conditions. Whether these chemical forces represent so-called primary or secondary valences is immaterial. Gases impinging upon the surfaces of solids or liquids did not in general rebound elastically, but condensed on the surface being held by the field of force of the surface atoms. The relative lengths of time these gases are held before evaporating determines the adsorption. The surface would become chemically saturated by a layer one molecule thick. Since the forces act between the atoms at the surface and par-

[1] *Jour. Amer. Chem. Soc. 38,* 2249 (1916).
[2] *Jour. Amer. Chem. Soc. 38,* 2249 (1916).
[3] *Jour. Amer. Chem. Soc. 39,* 1857 (1917).

ticular groups or atoms of the adsorbed molecules, the adsorbed molecules usually orient themselves in definite ways in the surface layer. Thus, oxygen adsorbed on a carbon filament is formulated as follows:



Similarly for carbon monoxide and tungsten:



Evidence based in the first instance upon the electron emission from heated metals showed that the adsorbed film was held to the surface by chemical forces, and consisted in all probability of a single layer of molecules; at most of a very few layers. It was found, for example, that substances which reacted with tungsten lowered the electron emission from it; inert gases did not. This view was then extended and applied to gases adsorbed on solids at ordinary pressures, and to adsorption in surface layers of liquids. It was pointed out that with gases and solids "the term adsorption should be restricted to gas taken up *on a surface* without any penetration of the gas molecules between the atoms or molecules on the solid surface." [1] In a subsequent paper on "The Adsorption of Gases on Plane Surfaces of Glass, Mica and Platinum," [2] the experimental work was extended and the theoretical explanations of the phenomena confirmed. It was pointed out that in the study of adsorbed films, much of the work described in the past involved the use of porous materials such

[1] *Jour. Amer. Chem. Soc.* *38*, 2284 (1916).
[2] *Ibid.* *40*, 1361 (1918).

as charcoal which made it difficult to determine the extent of the surface, that frequently because of the method of packing substances enormous numbers of capillary spaces might be formed in which with saturated or nearly saturated vapors, actual condensation of the liquid in the capillary spaces would occur, and that at times substances were used which actually dissolved the gas or vapor thought to be adsorbed, as, for example, water vapor in glass. The use of glass, mica, and platinum with a number of gases at low as well as at high pressures overcame these difficulties and made satisfactory quantitative measurements possible. The results obtained with these substances may be quoted.[1]

"It was found that at 100 bars' pressure the amounts of oxygen, nitrogen, hydrogen, carbon monoxide, carbon dioxide and argon adsorbed on glass or mica at room temperature were not measurable, although if 0.0002 of the surface had been covered by a layer one molecule deep it could have been readily detected. On cooling these surfaces to liquid air temperature the surfaces became covered with a monomolecular layer to the extent of 1 to 10 per cent and at 100 bars' pressure they seemed nearly saturated. The relatve amounts of different gases absorbed were in the same order as the boiling points, showing that the forces involved in this adsorption were secondary valence forces such as those involved in the liquefaction of these gases.

"With platinum surfaces the phenomena were totally different. Even at pressures below one bar the surface adsorbed hydrogen, carbon monoxide or oxygen immediately to form a layer covering the surface with a layer approximately one molecule (or atom) deep. These films could not be driven off by heating to 360°, but could be made to displace one another. The surfaces were wholly saturated at a few bars' pressure, and no increase in adsorption could be noted by raising the pressure to 200 bars. These films are evidently held to the platinum by primary valence forces.

"With the platinum at liquid air temperature the gases are first adsorbed by secondary valence forces, because when the temperature is raised to room temperature the gas first comes off the surface, and then at a temperature somewhat below room temperature goes back again onto the surface.

"In no case, however, was any adsorption noted which corresponded to a layer more than one moleclue deep."

The different conditions of adsorption were considered theoretically, and mathematical expressions developed which readily accounted for the adsorption formula usually employed.

The properties of the surface layers of liquids were treated by the same methods by Langmuir. His views, confirmed by all subsequent work, may be quoted from his first paper on the subject: [2]

[1] *Jour. Amer. Chem. Soc. 39*, 1904-5 (1917).
[2] *Met. Chem. Eng. 15*, 469 (1916).

"A theory of surface tension is now proposed in which the structure of the *surface layer of atoms* is regarded as the principal factor in determining the surface tension (or rather surface energy) of liquids. This theory is supported in the most remarkable way by all available published data on the surface tension of organic liquids.

"According to this theory, the group molecules of organic liquids arrange themselves in the surface layer in such a way that their active portions are drawn inwards, leaving the least active portion of the molecule to form the surface layer. By 'active portion' of a molecule is meant a portion which is characterized by a strong stray field (residual valence). Chemical action may be assumed to be due to the presence of electromagnetic fields surrounding atoms. Surface tension (or surface energy) is thus a measure of the potential energy of the electromagnetic stray field which extends out from the surface layer of atoms. The molecules in the surface layer of the liquid arrange themselves so that this stray field is a minimum.

"The surface energy of a liquid is thus not a property of the group molecules, but depends only on the *least active portions of the molecules* and on the manner in which these are able to arrange themselves in the surface layer.

"In liquid hydrocarbons of the paraffin series the molecules arrange themselves so that the methyl groups (CH_3) at the ends of the hydrocarbon chains form the surface layer. The surface layer is thus the same, no matter how long the hydrocarbon chain may be. As a matter of fact, the surface energy of all these many different substances from hexane to molten paraffin, have substantially the same surface energy, namely 46 to 48 ergs per sq. cm., although the molecular weights differ greatly.

"If, now, we consider the alcohols such as CH_3OH, C_2H_5OH, etc., we find that their *surface energies are practically identical with those of the hydrocarbons.* The reason for this is that the surface layer in both cases consists of CH_3 groups.

"With such substances as CH_3NO_2, CH_3I, we find that the surface energy is much greater than that of the hydrocarbons. This is due to the fact that the volume of the I or the NO_2 is so great that the surface cannot be completely covered by the CH_3 radicals. The forcing apart of these groups increases the surface energy.

"Particularly interesting relations are found with benzene derivatives.

"In benzene itself, the group molecules arrange themselves so that the benzene rings lie flat on the surface, since the flat sides of these rings are the least active portions of the molecules. The surface energy of benzene is about 65 ergs per square cm.

"If, now, an active group, such as OH, is substituted for one of the hydrogens of the benzene (forming phenol or carbolic acid) this group is drawn into the body of the liquid *tilting the benzene ring up on edge* and raising the surface energy to about 75 ergs per sq. cm., which corresponds to the activity of the perimeter of the benzene ring. Thus *any active* group strong enough to tilt the ring up on edge raises the surface energy to about 75. Two active groups side by side (ortho position) have no greater effect than one. But two active groups opposite one another (para position) cannot both go wholly below the surface, so that the surface energy then becomes abnormally large (about 85 in case of *p*-nitrophenol). The substitution of methyl or ethyl groups in the benzene ring lowers the surface energy except where an active group in an adjacent position draws these groups below the surface.

"Some of the best evidence in support of the new theory is derived from experiments on thin films of oil on water or mercury. Oleic acid on water forms a film one molecule deep, in which the hydrocarbon chains stand vertically on the water surface with the COOH groups in contact with the water.

"Acetic acid is readily soluble in water because the COOH group has a strong secondary valence by which it combines with water. Oleic acid is not soluble because the affinity of the hydrocarbon chains for water is less than their affinity for each other. When oleic acid is placed on water the acid spreads upon the water because by so doing *the COOH can dissolve in the water* without separating the hydrocarbon chains from each other.

"When the surface on which the acid spreads is sufficiently large the double bond in the hydrocarbon chain is also drawn down on to the water surface, so that the area occupied is much greater than in the case of the saturated fatty acids.

"Oils which do not contain active groups, as for example pure paraffin oil, do not spread upon the surface of water."

The adsorption of liquids by solids was treated on the basis of Gurvich's experiments.[1] Although Gurvich considered that the adsorption was not due to chemical forces, Langmuir[2] interpreted his results by means of the chemical theory outlined. In the adsorption of a liquid by a plane solid surface, the molecules of the liquid become oriented if active groups are present. There would therefore be a tendency for a simple integral relation to exist between the number of molecules adsorbed and the number of atoms exposed in the surface of the solid. With a crystal, in which the surface atoms are arranged in a regular lattice, stoichiometric relations might be expected to exist between the amounts of different liquids or gases needed to saturate the surface. The number of molecules which can be adsorbed on a given surface, evidently depends also upon the configurations of these molecules. This introduces a steric factor, which may be of considerable importance in some cases. This is true especially of adsorption by porous bodies, and as the cavities become smaller, stoichiometric relations would be less frequent.

It was pointed out that the forces causing adsorption being typically chemical, exhibit all the great differences in intensity and quality characteristic of chemical forces. "Under certain conditions stoichiometric relations should govern the amounts of gas adsorbed on saturated surfaces. These relationships may fail to hold because of steric hindrance effects between the adsorbed molecules.

"Equations are developed which give the relation between the amount of adsorbed gas and the pressure and other variables under various assumed conditions. No single equation other than purely thermodynamic ones should be expected to cover all

[1] L. G. Gurvich, *J. Russ. Phys.-Chem. Soc.* *47*, 805 (1915).
[2] *Jour. Amer. Chem. Soc.* *39*, 1898 (1917).

cases of adsorption any more than a single equation should represent equilibrium pressures for all chemical reactions." [1]

The possible occurrence of adsorbed layers on solids more than one molecule in thickness was not ignored by Langmuir, but was not considered to be adsorption in the strict sense of the word. He pointed out that such layers could be formed with nearly saturated vapors where the rate of evaporation from the second layer of molecules is comparable with the rate of condensation, and also if the forces acting between the first and second layers of adsorbed molecules were greater than those holding the first layer to the surface.

Views similar to those of Langmuir relative to the structure of the surfaces of liquids were developed independently and practically simultaneously by Harkins as a result of the study of surface tensions.[2] The work done in ergs per square centimeter when the surfaces of two liquids come together to form an interface was shown to be characteristic for each class of compound [3] The data clearly brought out the fact that the molecules of a number of liquids in contact with water were oriented so that the active group (also called the polar group) at the end of a hydrocarbon chain was in contact with the water. These "active" groups included OH, CHO, COOH, double bond, triple bond, CN, SO_3H, $CONH_2$, NO_2, NH_2, NCS, I, COR, SH, etc. The surfaces of such liquids therefore show a structure. A general law was stated as follows: "If we suppose the structure of the surface of a liquid to be at first the same as that of the interior of the liquid, then the actual surface is always formed by the orientation of the least active portion of the molecule toward the vapor phase and at any surface or interface the change which occurs is such as to make the transition to the adjacent phase less abrupt." It was pointed out that the fundamental idea developed is the same as that developed by Langmuir, namely, "that surface tension phenomena in general are dependent upon the orientation and packing of molecules in surface layers, and that the forces involved

[1] *Jour. Amer. Chem. Soc. 40,* 1401 (1918).

[2] W. D. Harkins and co-workers, *Jour. Amer. Chem. Soc 39,* 354, 541 (1917); *41,* 970 (1919); *42,* 700 (1920). Cf. also W. C. Reynolds, *J. Chem. Soc. 119,* 460, 466 (1921).

[3] In this connection, as well as for the first suggestion of a possible orientation of molecules in liquid surfaces, cf. W. B. Hardy, *Proc. Roy. Soc. London (A) 88,* 303 (1913). Cf. also the experimental study of H. R. Kruyt and C. F. van Duin, *Rec. Trav. Chim. Pays-Bas 50,* 249 (1921).

in this action are related to those involved in solution and adsorption."

These views on structures of surfaces and surface films indicate a general solution of the problem of contact reactions as well as of contact catalytic reactions. The formation of chemical compounds on the surface is the first step in such reactions. These compounds are due to chemical forces (valence forces). In plane solid surfaces, with an adsorbed film, the latter would ordinarily be one atom or molecule thick. Quantitative studies are possible in such cases. With porous materials, or with nearly saturated vapors where liquefaction is possible, quantitative comparisons cannot be carried out so readily. The realization that adsorption compounds are based upon the same chemical forces which are involved in the production of other chemical compounds makes possible a rational study and, it may confidently be expected, a rational understanding of such compounds.

Before speaking of contact reactions farther, it may be well to speak of a factor which, to the writer at any rate, does not appear as yet to have been accounted for in a satisfactory manner. This factor is the part which is played by some chemical combining force in various phenomena. As stated previously, Langmuir defined primary valence and secondary valence in a way which did not indicate any essential difference between the two, but in the discussions and applications he used them to represent different phenomena which in many cases showed definitely different behaviors. He apparently considered that the transfer of an electron to form a definite electron grouping or configuration in an atom or molecule involved a primary valence, while stray fields of force due to electrons forming the outer shells of atoms cause secondary valence effects. In this connection, it may be mentioned that electrical attraction has been assumed at various times to play a part in the formation of chemical compounds, or in some of the phenomena observed in the formation or reactions of such compounds. Thus, A. A. Noyes[1] in connection with the anomalies observed in solutions of highly ionized electrolytes spoke of electrical molecules and chemical molecules, the existence of the former being due to electrical attraction between electrically charged atoms; J. M. Nelson and

[1] A. A. Noyes, *Jour. Amer. Chem. Soc. 30,* 351 (1908).

the writer [1] indicated the possibility of considering J. Thiele's partial valences on the basis of the electron conception of valence as due to the electrical charges on atoms resulting from their unions with other atoms; E. C. C. Baly [2] developed a theory of the mechanism of chemical reactions on the basis of condensed force fields of electromagnetic type surrounding chemical molecules; and a number of others might be quoted who suggested similar views. Langmuir considered such a force field involved in the phenomena which he denoted as due to secondary valences, while Harkins and King [3] developed a similar hypothesis and applied it to the distribution of a solute between various phases as conditioned by the intermolecular electromagnetic fields.

These phenomena of chemical combination form the uncertain note in the explanation of certain adsorption phenomena, such as the adsorption of some of the so-called permanent gases by solids, while at the same time many other cases of adsorption were found to be due to "primary" or ordinary valence forces. It must be emphasized, however, that such surface phenomena, whether explained as due to secondary valence forces, or to the actions of electromagnetic fields, or to any other cause, are also well known among chemical compounds and reactions aside from those classed as adsorption and have been explained by the terms secondary valence, auxiliary valence, electrical attractions of various kinds, force fields, etc. Without attempting to account for the actions of these chemical forces in any final and definite manner, it may be said that the forces acting to form these adsorption compounds differ in no way from the forces which have been observed in other reactions. Their interpretation is not as direct at the present time as the interpretation of the chemical unions which involve definite changes in the positions of electrons, but it appears probable that an explanation for the former will be found in the configurations or in changes in the configurations of the electrons in the adsorbed molecules or atoms and the adsorbing surface. An explanation involving such views was suggested by Harkins and King. At any rate, the state-

[1] K. G. Falk and J. M. Nelson, *Jour. Amer. Chem. Soc. 32*, 1650 (1910).
[2] Cf. *Jour. Amer. Chem. Soc. 37*, 979 (1915).
[3] W. D. Harkins and H. H. King, *Jour. Amer. Chem. Soc. 41*, 970 (1919).

ment which has been made repeatedly is not modified by these considerations, that the forces acting in adsorption phenomena are identical with those acting in the formation and reactions of chemical compounds in general.

The application of these adsorption views to chemical reactions taking place in heterogeneous systems is obvious in principle. The following general statement of Langmuir [1] may be used as the basis: "In a heterogeneous chemical reaction, the activity of a surface depends in general upon the nature of the arrangement of, and spacing of the atoms forming the surface layer." It is of interest to mention in passing, the earlier attempts, from which were developed these later views, to formulate a general theory of heterogeneous or contact reactions. Noyes and Whitney [2] studied the solution of a solid in a liquid. The rate was found to depend upon the rate of diffusion of the saturated solution into the rest of the liquid, the reaction between solid and liquid (dissolving of solid in liquid) being extremely rapid. Nernst [3] extended this conception to include all reactions occurring in heterogeneous systems. He considered that the equilibrium at the surface of two phases was set up very rapidly, practically instantaneously, in comparison with the velocity of diffusion. Since the equation representing the velocity of diffusion was similar in form to the equation of a monomolecular reaction, whenever the latter appears to hold for a reaction taking place in a heterogeneous system, it is probable that the reaction velocity measured is that of a rate of diffusion. This simple view was extended by Fink,[4] who showed that in the mechanism of heterogeneous reactions, the reaction velocity was limited by the rate of diffusion of the reacting substances to the surface where the reaction was taking place through an adsorbed film of variable thickness of the substances taking part. The view of Langmuir postulates that the velocity of heterogeneous reactions is controlled primarily by the rate at which the molecules strike against that portion of the surface which is active. It was recognized that physical factors such as rates of diffusion through layers of gas or through films may

[1] I. Langmuir, *Jour. Amer. Chem. Soc.* **37**, 1142 (1915).
[2] A. A. Noyes and W. R. Whitney, *Z. physik. Chem.* **23**, 689 (1897).
[3] W. Nernst, *Z. physik. Chem.* **47**, 52 (1904).
[4] C. G. Fink, Dissertation, Leipsig, 1907; M. Bodenstein and C. G. Fink, *Z. physik. Chem.* **60**, 1, 46 (1907).

modify the conditions or limit the chemical reaction occurring, but these factors were considered to be of secondary importance in most cases. The velocity of a reaction then usually depends on the fraction of the surface covered by adsorbed atoms or molecules, which in turn depends on the rate of condensation and on the rate of evaporation (for gases, and corresponding rates for liquids) of the adsorbed substance. This conception was developed in mathematical form to cover certain special cases after making some simplifying assumptions. A "law of surface action" was obtained analogous to the "law of mass action." The action of a "poison" was shown to consist of the formation of a very stable film one atom or molecule deep.

It will not be necessary to enter farther into the theory and mathematical deductions given by Langmuir. The view which he presented of the mechanism of contact reactions is clear and without question the most satisfactory available at the present time. At the same time, the conclusions have been applied quantitatively to comparatively few reactions. On the other hand, this theory offers the best method which has been proposed for classifying contact reactions without introducing new and unknown factors and for this reason has been outlined here. Also, it brings out clearly the connection between the mechanism of contact reactions and the mechanism of chemical reactions in general which was outlined in the earlier chapters. Both are based upon the primary formation of intermediate or addition compounds of the reacting substances. If one of the substances in a contact reaction possesses the same chemical composition before and after the reaction, then the reaction would be classed as contact catalysis. In many reactions in which the gaseous components are changed chemically, a substance in the solid state is involved, which sometimes acts as the container, but is unchanged in composition at the end of the reaction. Such reactions are included in contact catalysis and form probably the principal reactions of that group. The general formulations given in the earlier chapters to represent the mechanism of chemical reactions are directly applicable to contact reactions.

Because of the importance of the theoretical views of Langmuir, some of his experimental work may be given first. His

earlier work on chemical reactions at low pressures [1] included the "clean-up" of a gas by a heated filament. The four types of reaction studied included the direct attack of the filament by the gas (tungsten and oxygen or chlorine, carbon and oxygen); the action of the gas with the vapor given off by the filament (tungsten and nitrogen or carbon monoxide, molybdenum and nitrogen, platinum and oxygen); the catalytic action of the filament on the gas, producing a chemical change in the gas without any permanent change in the filament (dissociation of hydrogen, chlorine, and oxygen into atoms by heated tungsten, platinum, or palladium, as well as other chemical changes); and complicated reactions in which electrical discharges ionized the gas and brought out reactions between ionized gas and filament (tungsten and nitrogen). These reactions were all readily explained by means of the theory of chemical combination (with the filament or other body) as already outlined. A more detailed study was made of the action of carbon monoxide and oxygen and of hydrogen and oxygen with platinum. The results were summarized as follows: [2] "No adsorption of gases could be observed even at — 183°, until the platinum had been "activated" by heating to 300° in a mixture of hydrogen and oxygen at low pressure. After this activation, hydrogen and oxygen and carbon monoxide and oxygen reacted together readily at room temperature in contact with the platinum. The platinum was then found capable of adsorbing oxygen, carbon monoxide or hydrogen. The maximum quantities of oxygen and carbon monoxide corresponded to monomolecular layers. The oxygen could not be driven off either by heat or by pumping. When the platinum was in contact with an excess of oxygen the amount of oxygen adsorbed increased as the temperature was raised, but the action was irreversible. Adsorbed carbon monoxide could not be removed at room temperature, but at 300° part of it could be pumped off. When oxygen was brought in contact with carbon monoxide adsorbed on the platinum it reacted rapidly to form carbon dioxide which at room temperature showed no tendency to be adsorbed on the platinum. In a similar way carbon monoxide brought into contact with adsorbed oxygen reacted

[1] I. Langmuir, *Jour. Amer. Chem. Soc.* **37**, 1139 (1915).
[2] I. Langmuir, *Jour. Amer. Chem. Soc.* **40**, 1402 (1918).

immediately. These cases of adsorption are clearly due to chemical forces of the primary valence type. Further work needs to be done to determine the cause of the activation of the platinum."

If a gas forms an adsorbed film on a surface, for example platinum, and if the gas evaporates slowly, a platinum surface would no longer be present. The catalytic activity of the platinum would be lost, or the catalyst is said to have been poisoned. Arsenic, antimony and phosphorus have this effect; evidently they are combined with the platinum and do not evaporate at an appreciable rate. Cyanogen and carbon monoxide have similar, though more transient effects on platinum; they "poison" the platinum only as long as some of the substance is present in the gaseous phase. If a reaction takes place in the presence of a gas which has a poisoning action on the catalyst, the velocity will depend on the fraction of the surface not covered by the molecules of the poisoning gas.

"When gas molecules condense on a solid surface in such a way that they are held on the surface by primary valence forces, involving a rearrangement of their electrons, their chemical properties become completely modified. It is not surprising, therefore, that in some cases such adsorbed films should be extremely reactive, while in other cases they may be very inert to outside influences. Thus oxygen adsorbed on platinum reacts readily with hydrogen or carbon monoxide, while oxygen on tungsten, or carbon monoxide on platinum, show very little tendency to react with gases brought into contact with their surfaces. The specific nature of the behavior of these various films is quite consistent with the theory that the adsorption depends on typical chemical action. In many cases, especially where we deal with adsorption of large molecules, the orientation of the molecules on the surface is a factor of vital importance in determining the activity of the surface towards reacting gases."[1]

Langmuir also considered the effect of treatment on a surface. For example, the occurrence of a reaction, or rapid heating and cooling as by an alternating current, roughens the surface of metals such as platinum, etc. In this way the surface area becomes larger and a greater number of favorable locations for action is produced. At the same time the significant fact must be noted that the surface may become activated for one reaction and not for another. Thus, a plane surface of platinum activated (lowering of temperature at which reaction began) toward the hydrogen-oxygen reaction by a single treatment at

[1] I. Langmuir, *Chem. News* **123**, 225 (1921).

low pressures with a hydrogen-oxygen mixture was not activated toward the carbon monoxide-oxygen reaction.[1]

These results showed clearly the chemical nature of the forces involved in these adsorptions and contact actions. Even with these comparatively simple reactions, the mechanism of the changes may be quite complex and present features which have not been satisfactorily elucidated. Some recent work on the hydrogenation of aromatic compounds with the aid of platinum or palladium[2] also indicated that the "activation" of these metals might involve a more complex change than is apparent at first sight. Catalytic hydrogenation was found to depend on the presence of oxygen; the intermediate products were not hydrides but contained both oxygen and hydrogen. Completely deoxygenated palladium sponge or colloidal palladium was found to be incapable of hydrogenating even such compounds as diolefins.

One of the most important features of chemical compounds is their individuality. Each atom or molecule will act in a more or less specific way with various reagents. The reactions which are used in qualitative and quantitative chemical analyses take advantage of these differences. Certain reactions which are grouped under contact catalysis have been used in quantitative analysis. The reactions to which reference is made especially are the so-called "preferential combustion" reactions, in which gaseous mixtures may be analyzed by fractional or partial combustion (oxidation) of the constituents. The separate estimations of hydrogen and methane may be quoted as illustrating the possibilities of such reactions.[3] If a mixture of hydrogen and methane is passed over cupric oxide at 250°, the hydrogen will be oxidized completely while the methane will not be attacked. The use of cupric oxide is stated to be preferable to that of palladium or palladinized asbestos because the addition of air or of oxygen is obviated. Also, hydrogen is oxidized before methane at comparatively low temperatures in contact with

[1] For further evidence relative to these phenomena cf. P. Woog, *Compt. rend. 173*, 387 (1921); N. K. Adam, *Proc. Roy. Soc. London (A) 99*, 336 (1921); H. S. Taylor and R. M. Burns, *Jour. Amer. Chem. Soc. 43*, 1273 (1921); H. S. Taylor and H. A. Neville, *Jour. Amer. Chem. Soc. 43*, 2055 (1921).

[2] R. Willstätter and E. Waldschmidt-Leitz, *Ber. 54B*, 113 (1921). Cf. however C. Kelber, *Ber. 54B*, 1701 (1921).

[3] Cf. W. D. Bancroft, *J. Physic. Chem. 21*, 644 (1917), for a summary of reactions involving fractional combustion of gases.

platinum, or at higher temperatures if the mixture of gases is passed through a platinum tube. Methane is found to be oxidized in preference to hydrogen at moderate temperature in borosilicate glass bulbs and if the mixture of gases is fired by an electric spark.

Similar preferential combustion reactions have been studied for mixtures of gases containing hydrogen, carbon monoxide, various hydrocarbons, etc., involving the use of a number of metals or oxides. A satisfactory review of such reactions together with references to the original papers was given recently (1919) by E. K. Rideal and H. S. Taylor in their book on "Catalysis in Theory and Practice." [1]

The question of hydrogenation reactions in general belongs to the reactions under discussion. The reactions described and summarized by P. Sabatier, who did a great deal of the work himself, in his book [2] on "La Catalyse en Chimie Organique" included in the main, contact catalytic reactions. He assumed, as the most probable explanation for the mechanism of such reactions, the formation of an intermediate compound of catalyst with the reacting substances. A similar, but perhaps more definite point of view was developed by E. F. Armstrong and T. P. Hilditch in a series of studies on "Catalytic Actions at Solid Surfaces" [3] in which various metals were used in hydrogenation reactions. Some of their statements are pertinent to the problem under discussion. For example, they adopted the theory of the formation of unstable intermediate compounds in such reactions, and considered the physical view of adsorption (as dependent upon chemical forces) to be identical with the chemical hypothesis of unstable intermediate compounds; [4] that "the primary action of the catalyst in all these cases is to effect an association with the carbon compound, the resulting unstable complex then being resolved into other compounds"; [5] that the activity of the catalyst (nickel in the special case under investigation) de-

[1] Pp. 439-446. The recent studies by C. Conover and H. D. Gibbs (*J. Ind. Eng. Chem.* *14*, 120 (1922) on the oxidation of naphthalene to phthalic anhydride by air in the presence of various oxides at higher temperatures may also be mentioned. Vanadium pentoxide was found to give the best results; molybdenum trioxide gave fairly good results; while a large number of other oxides were found to be poor or worthless for the purpose.

[2] Published in 1913; second edition, 1920.

[3] Published in *Proc. Roy. Soc. London*, 1919-1921.

[4] *Proc. Roy. Soc. London* (*A*) *98*, 27 (1920).

[5] *Ibid.* *97*, 259 (1920).

pended upon a suitable surface and the specific nature of the catalyst in being able to form appropriate intermediate compounds with the reacting substances; [1] etc.

A number of additional workers might be quoted to the same effect [2] relative to reactions similar to those described, but this would not add to the general point of view outlined. The mechanisms of the reactions can evidently be accounted for readily according to the principles developed even if exact quantitative data are not always available. It will perhaps be of more interest to take up reactions of somewhat different nature or involving chemical changes different from those heretofore considered.

The decomposition of ethyl alcohol may take place according to the following reactions as indicated in Chapter III:

$$\left[C_2H_5OH\right] \begin{matrix} = H_2O + C_2H_4 & \text{(a)} \\ = H_2 + CH_3CHO & \text{(b)} \end{matrix} \qquad (1)$$

A study of the products obtained when alcohol was heated in the presence of a number of oxides and of metals gave the following results:[3] In the presence of thorium oxide (all the oxides were prepared at temperatures below 350°) at 340–350°, the reaction followed equation (a) exclusively; with aluminium oxide or tungstic oxide (blue), the reaction followed (a) almost entirely, very little hydrogen (1.5% by volume of gas) being formed; with chromium oxide, silica, or titanium oxide, the reaction took place according to both equations with (a) predominating; with beryllium oxide or zirconium oxide about one-half of the decomposition followed each equation; with uranium oxide, molybdenum oxide (blue), ferric oxide, vanadous oxide, or zinc oxide, considerably more of the products of equation (b) than of equation (a) were formed; while with manganese dioxide, stannous oxide, cadmium oxide, manganous-manganic oxide (Mn_3O_4), magnesium oxide, or finely divided nickel or copper, the reaction took place entirely according to equation (b). The reaction according to equation (b) was complicated in some cases by the decomposition of the acetaldehyde into methane

[1] *Proc. Roy. Soc. London* (*A*) *99*, 490 (1921).
[2] Cf. H. Euler and A. Hj. Hedelius, *Arkiv. Kemi, Mineral Geol.* 7, No. 31 (1920).
[3] P. Sabatier and A. Mailhe, *Ann. chim. phys.* (*8*) *20*, 289 (1910).

and carbon monoxide. The efficiency of these substances as catalysts varied greatly, the gases evolved per minute under the experimental conditions used ranging from traces with magnesium oxide and 0.9 cubic centimeter with silica up to 57 cubic centimeters with tungstic oxide and 110 cubic centimeters with copper. A study [1] of the addition of water vapor and of hydrogen to the reaction mixtures showed some definite influences on the displacement of the equilibria with the different catalysts, but some more recent results indicate that further studies [2] of the mechanism of the reactions, perhaps similar to those carried on by Langmuir with different reactions, are necessary in order to account for the observed effects.

Similar decompositions have been described with other alcohols. Thus, isobutyl alcohol at 300° formed isobutyl aldehyde and hydrogen in the presence of copper, isobutylene and water in the presence of aluminium oxide, and both the aldehyde and isobutylene in the presence of uranium oxide.[3] The results with allyl alcohol have also been published.[4]

Formic acid may decompose according to the following equations: [5]

$$\left[\mathrm{HCO_2H}\right] \begin{matrix} = \mathrm{H_2O} + \mathrm{CO} & \text{(a)} \\ = \mathrm{H_2} + \mathrm{CO_2} & \text{(b)} \end{matrix} \qquad (2)$$

Reaction (a) takes place on warming formic acid with sulfuric or other mineral acids, reaction (b) by heating formic acid with platinum or with finely divided rhodium, ruthenium, or iridium, or with an excess of alkali. A recent study of the decomposition of salts of formic acid by heat, or by passing formic acid vapor over heated metallic oxides where the first products formed were the metal formates which then decomposed, gave some interesting results.[6] The reaction primarily was considered to be as follows:

$$(\mathrm{CHO_2})_2\ \mathrm{Me''} = \mathrm{MeCO_3} + \mathrm{HCHO}, \qquad (3)$$

[1] C. J. Engelder, *J. Physic. Chem.* *21*, 676 (1917).
[2] W. D. Bancroft, Address on "Contact Catalysis," American Electrochemical Society, 1920.
[3] P. Sabatier, "La Catalyse en Chimie Organique," German translation, 1914, p. 240.
[4] P. Sabatier and B. Kubota, *Compt. rend.* *173*, 17, 212 (1921).
[5] Cf. Chapter III, p. 41.
[6] K. A. Hofmann and H. Schibsted, *Ber.* *51*, 1398 (1918).

in which the nature of the contact substance or metal oxide, formate, or carbonate, as well as the manner of heating, water content, and other factors, determined the various further changes which took place. With zinc formate, a yield of 25 per cent of formaldehyde could be obtained; with lithium formate (perhaps partly because of the high temperature required to cause decomposition) very little formaldehyde was found, the main products being acetone, methyl alcohol, furfurol, pyruvic acid, and charcoal. Lead formate gave formaldehyde and much methyl alcohol; cobalt formate, only traces of methyl alcohol; aluminium formate, no formaldehyde or methyl alcohol; stannous formate, a good yield of formaldehyde and almost no methyl alcohol; etc. The results were given for a number of additional salts and the effects of varying the conditions, such as temperature, addition of various substances to the reaction mixture, etc., carefully studied. The apparent irregularity of the results made it difficult to draw any general conclusions relative to the reasons for the different actions of the different salts.

The decomposition of ethyl acetate, when heated with different solid catalysts, may proceed according to the following equations:

$$\left.\begin{array}{l} \\ n\mathrm{CH_3CO_2C_2H_5} \\ \\ \end{array}\right\} \begin{array}{ll} = \mathrm{CH_3CO_2H} + \mathrm{C_2H_4} & \text{(a)} \\ = \mathrm{CH_3CH_2CH_3} + \mathrm{CO_2} & \text{(b)} \\ = \mathrm{CH_3COCH_3} + \mathrm{CO_2} + \mathrm{C_2H_5OH} + \mathrm{C_2H_4} & \text{(c)} \end{array}$$

(4)

Reaction (a) takes place in the presence of titanium oxide; reaction (b) with finely divided nickel; and reaction (c), with thorium oxide.[1] According to Langmuir's view, the —CO.O— group is probably attached to the catalyst surface by means of ordinary valences, and, "depending upon the different manners in which interaction between atoms and evaporation may occur, the resulting products differ." [2]

The results obtained with some simple compounds of nitrogen may be quoted.[3] Hydroxylamine in a hot alkaline solution

[1] These results were obtained by Sabatier. The recently published work of H. Adkins and A. C. Krause (*Jour. Amer. Chem. Soc. 44*, 385 (1922)) indicates that these conclusions require revision.

[2] I. Langmuir, *Chem. News 123*, 237 (1921).

[3] S. Tanatar, *Z. physik. Chem. 40*, 475 (1902).

was found to decompose mainly according to the following equation:

$$3NH_3O = NH_3 + N_2 + 3H_2O \qquad (5)$$

In the presence of platinum black, however, the reaction proceeded principally as follows:

$$4NH_3O = 2NH_3 + N_2O + 3H_2O \qquad (6)$$

The actions of the alkali in the reaction shown in equation (5) and of the platinum black in the reaction of equation (6) are not given in these equations. Only the latter would represent a case of contact catalysis.

It is difficult at the present time to say more relative to these reactions. The nature of the catalysts and the conditions under which the changes are allowed to take place evidently play a most important part in determining the character of the products. It is especially clear, in considering such reactions as the above, that the catalyst plays an active part in these chemical reactions, and that an understanding of the mechanism of the changes involves necessarily the participation of the catalyst in the reaction and the representation of this participation in the chemical equation which is supposed to indicate the changes taking place, as well as in all other equations or expressions which may be intended to be descriptive of the reactions in question.

It would be possible to extend the list of contact catalytic reactions and to discuss the possible mechanism of the changes on the basis of the data of various kinds which are available. The reactions which have been given are only a few of those which might be given, and perhaps not the most important, nor, from some points of view, the most interesting. Thus, the Haber process of ammonia synthesis, the contact sulfuric acid process, the recent striking developments of the application of silica gel to a variety of processes (the latter, however, being essentially condensation phenomena), etc., would permit of almost unlimited discussion. These reactions, and especially the first two, have been taken up in detail in various connections in the chemical literature. As far as the writer is aware, no new principles have been developed in the study of these reactions,

differing from those outlined here. An enumeration of additional reactions, therefore, which might be included under Contact Catalysis will be dispensed with in this connection.

The term "promoter" action in catalysis has been used to indicate the influence of various substances in increasing the actions of catalysts. In a recent review entitled "Promoter Action in Catalysis," Pease and Taylor[1] made a distinction between (1) Activation of a catalyst by a substance relatively inert catalytically or by a small quantity of relatively inactive substance, and (2) Co-activation of two or more catalytically active substances each by the others. They gave neutral salt actions in catalyses by hydrogen ions in aqueous solutions, etc., as examples of the first group of actions, and the actions of iron and of molybdenum and of a mixture of the two on the ammonia synthesis from nitrogen and hydrogen as an example of the second. A number of reactions might be quoted to illustrate this promoter action. For example, the oxidation of carbon monoxide to carbon dioxide by the oxygen of the air at ordinary temperatures by a mixture of three or four oxides is a case in point;[2] the increased hydrogenation of fats by the addition of tellurium to nickel; etc.[3]

In view of the striking character of some of these promoter actions, it is surprising that no theory, based upon experimental evidence, has so far been suggested which accounts for these actions in a satisfactory way.

The enzyme actions which were described in Chapter VI belong at least in part to the group of contact catalytic reactions. All enzymes, as far as known, are associated with, or form part of, matter in the colloid state. Even when the solutions containing enzymes appear to be clear to the eye, as with some sucrase and esterase preparations, the enzyme substance is not able to pass through a suitable semi-permeable membrane such as collodion or parchment, while, to go to the other extreme, a number of enzymes are practically insoluble and can be separated from their solutions or mixtures by means of simple fil-

[1] R. N. Pease and H. S. Taylor, *J. Physic. Chem.* **24**, 241 (1920).

[2] A. B. Lamb, W. C. Bray, and J. C. W. Frazer, *J. Ind. Eng. Chem.* **12**, 213 (1920); T. H. Rogers, C. S. Piggot, W. H. Bahlke, and J. M. Jennings, *Jour. Amer. Chem. Soc.* **43**, 1973 (1921); D. Merrill and S. C. Scalione, *Jour. Amer. Chem. Soc.* **43**, 1982 (1921).

[3] Cf. E. K. Rideal and H. S. Taylor, "Catalysis in Theory and Practice," 1919, pp. 29-32, for additional examples.

tration through ordinary filter paper. These also show colloidal properties. The question which may be raised relates to the extent to which the views on contact reactions apply to enzyme actions. The summary of the results of the study of enzyme actions presented in Chapter VI as well as the relations pointed out in other connections [1] falls in with the chemical relations developed by Langmuir although the question of the nature of the surface actions is not directly applicable, or at least not well enough defined at the present time. The first step in the action between enzyme and substrate is a chemical combination between the two to form the so-called addition compound. Because of the colloidal nature of the enzyme preparations as well as the colloidal nature of a number of the substrates which are used in enzyme studies, this action frequently has been considered to be an "adsorption" phenomenon with the chemical forces playing at most a secondary part.[2] The view of Langmuir relative to the part played by chemical forces in forming adsorption compounds brings the two explanations together. The limiting amount of substrate with which a definite (small) amount of enzyme can react in a unit of time is also suggestive of the extent of surface which can be covered by the adsorbed substance. Both are fundamentally perhaps only different forms of the law of definite proportions in chemical combinations. Further, the combination of the products of an enzyme action with the enzyme prevents the further action of the enzyme on fresh substrate. This, also, is comparable to the "poisoning" of a surface by the adsorption by chemical forces, of a substance which, by covering the surface completely or even to a large extent, prevents different substances from reaching the surface and reacting with the catalyst substance and with each other. Enzyme actions and contact actions on solid surfaces can be treated from the chemical point of view as chemical reactions which are apparently somewhat more complex than those ordinarily dealt with, as, for example, reactions in aqueous solutions. The apparent complexity is due in part to the fact that the former reactions involve substances present initially in different phases and also possibly be-

[1] Cf. "The Chemistry of Enzyme Actions."
[2] Cf. for example Chapter VII on "The Mode of Action of Enzymes" in "The Nature of Enzyme Action," by W. M. Bayliss; Fourth Edition; 1919.

cause these reactions take place in stages whose velocities frequently are of the same order of magnitude. It might be expected, because of their colloid nature and the reactions taking place in heterogeneous systems, that the actions of enzymes would be treated theoretically in the same way that contact reactions have been treated. As a matter of fact, in his treatment of contact phenomena, Langmuir [1] presented a brief outline in which he applied his views to enzyme actions, but made some additional assumptions with regard to the mechanism of the actions. J. M. Nelson and W. C. Vosburgh [2] pointed out the limitations of these assumptions, at least with respect to the action of sucrase, but in all probability applying also to other enzyme actions. In fact, it is doubtful whether such a general treatment as that indicated by Langmuir could state more than possible empirical rules of action, unless the chemical natures of the reacting substances are introduced. This last unfortunately appears to be almost impossible at the present time in view of the unknown chemical configurations of enzyme molecules and the uncharacterized physical structures of the surfaces of enzyme preparations.

Reactions which occur in heterogeneous systems are of interest in connection with changes which occur in living matter as indicated in the preceding chapter. The question of the phenomena which occur in or at the surfaces of cells, in which the cell walls or membranes play a part, appears to be related to the problems which have been taken up in this chapter relative to contact actions. Only a few of the possibilities can be mentioned here.

The question of osmosis and the existence of so-called semipermeable membranes and their actions is involved in these considerations. This is not the place to enter into a detailed discussion of these phenomena although they are of fundamental importance for an understanding of the relations as far as they have been developed.[3] Only a few of the more salient points can be taken up. In the first place, the process by which such

[1] I. Langmuir, *Jour. Amer. Chem. Soc. 38*, 2291 (1916).
[2] J. M. Nelson and W. C. Vosburgh, *Jour. Amer. Chem. Soc. 39*, 805 (1917).
[3] Cf. especially the studies of J. Loeb published in *J. Gen. Physiol.* 1919-1921.

a membrane acts has been studied extensively. In his monograph on "Osmotic Pressure," Findlay stated: [1]

> "The explanation of semi-permeability of membranes which is probably the most widely accepted at the present day, is that of selective or preferential solubility. The membrane is permeable to those substances which dissolve in it, and is impermeable to those substances which are insoluble in it."

This view shows that some form of combination is involved between a substance and a membrane when that substance is capable of passing through the membrane. Further, it is possible that the actions may be of the nature of adsorption as defined by Langmuir instead of solution as stated. The structures of membranes, being of more or less porous character, would make it difficult to decide, without careful study, which phenomenon was taking place. In fact, the whole problem appears to rest upon the specific properties of membranes. A thorough review, with references to the original literature, was given by W. M. Bayliss in his "Principles of General Physiology," [2] Chapter V, on "The Permeability of Membranes and the Properties of the Surface of Cells," to which reference may be made for more detailed information.

The cell membrane, if formed of different materials from the cell contents (possibly cellulose in the case of plant cells) or the cell surface which may be formed from the protoplasm of the cell, which, because of the surface energy, or of force fields at the surface due to the arrangements of atoms at the surface resulting for one thing in a change of surface energy, as postulated by Langmuir and by Harkins, would show the phenomena of contact actions toward foreign substances, which were described in the earlier parts of this chapter. A substance would combine with the membrane or surface because of chemical forces. The reactions would be specific. The further behavior of the combined substance might involve reaction with the protoplasm in the interior of the cell, or reaction with the substance of the cell surface, or possibly other changes. In view of the lack of definite knowledge of these phenomena at the present time, it would be idle to enter farther into these questions. The

[1] Monographs on Inorganic and Physical Chemistry: "Osmotic Pressure" by A. Findlay; published by Longmans, Green and Co., 1913. P. 68.
[2] Published by Longmans, Green & Co., 1915.

reactions are fundamentally contact reactions. If the cell membrane or surface is unchanged after the reaction, the change would be classed as contact catalysis.

These considerations do not touch upon the actions of the cell enzymes upon the material supplied to and taken up by the cells. There would appear to be a connection or interdependence, necessarily, between the "permeability" of the cell surface for certain substances and the character of the substances which can react with the enzyme within the cell. The life process of the organism may well depend upon this correlation. The study of the properties of cell surfaces or membranes would therefore be an essential part of the study of enzyme actions within the cells for a proper understanding of the chemical phenomena of life processes.

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